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An electro-anatomical study in the cat

By
JAN JANSEN JR.

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Preface

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Introduction

In spite of the rapid development in recent years in the field of cerebellar physiology, comparatively little new information is available concerning the cerebellar hemispheres and, in particular, concerning possible functional differences between the different lobules of the cerebellar hemisphere.* Most recent investigators have concentrated their attention upon the anterior lobe, the functional rôle of which seems better understood to-day than that of the hemispheres (Moruzzi 1950). The present investigation was started on the presumption that a more detailed knowledge of the afferent connections of the various subdivisions of the cerebellar hemispheres might result in a clearer understanding of their functional rôles. As recently stressed by Jansen (1950) and Jansen and Brodal (1954) it was felt that this was especially true with regard to the paraflocculus.

The structure and synaptology of the cerebellar cortex, which is uniform all over, is comparatively well known (Cajal 1911; Scheibel and Scheibel 1954). The cerebellar cortex, therefore, should prove favourable for an electrophysiological analysis of the origin of the different components of the evoked potentials. Some information might also possibly be obtained concerning the mode of operation of the cerebellar cortex.

The purpose of the present study was first to examine the characteristics and distribution of the potentials in the cerebellar hemispheres evoked by single shock stimulation of the cerebral cortex (chapter III, parts A and B), and then, to determine the pathways

* The term cerebellar hemisphere, as used here, comprises the paraflocculus, the ansoparamedian lobule, and the hemispheral parts of the lobulus simplex and the anterior lobe.

mediating these impulses (chapter III, part C). Finally, some observations were made on the potentials evoked in the cerebellar hemisphere following stimulation of some of the brain stem nuclei (pons, inferior olive, periaquaeductal gray, chapter IV). The lobulus simplex and the hemispheral part of the anterior lobe are not included in the present study as these cerebellar subdivisions have been investigated rather extensively in connection with the rest of the anterior lobe.

Chapter I

Previous studies on the afferent connections to the cerebellar hemisphere

(1) Electro-physiological studies

The first investigation of the electrical activity of the cerebellar hemispheres in response to afferent impulses was carried out by Beck and Bikeles (1912a). These investigators recorded changes in the electrical activity of crus II and the paramedian lobule following local heating of the contralateral pericruciate cortex of dogs. They also elicited activity in the paramedian lobule in response to electrical stimulation of peripheral nerves (Beck and Bikeles 1912b).

Dow (1939) recorded action potentials in the cerebellar hemispheres following stimulation of the pontine nuclei, the inferior olive and "dorsal reticular formation" in cats. This author also observed responses in the paramedian lobule evoked by stimulation of spinal nerves. As a possible explanation for the difference in the form of the potentials evoked from, for instance, the olive and the pons, he suggests that one type of impulse may be mediated to the cerebellar cortex via mossy fibres, another via climbing fibres.

Curtis (1940) recorded action potentials in the cerebellum of cats following stimulation of the cerebral cortex. Dow (1942) confirmed and extended this study. In the cat cerebellar responses were elicited in the culmen, lobulus simplex, lobulus ansiformis, declive and tuber vermis, paraflocculus and pyramis after stimulation of a rather extensive continuous area including the sigmoid, coronal, anterior ectosylvian and anterior parts of the lateral, suprasylvian and middle ectosylvian gyri. Dow concluded that no cortical subdivision appeared to be represented exclusively or even predominantly in any cerebellar lobe. Dow also described two components of the cortico-cerebellar action potentials. The more common response consisted of a long-latency (25 msec.) sharp deflection. If the

strength of the stimulating shock was increased a short-latency (3 msec.) wawe would frequently appear. Dow presumed, without any experimental verification, that both components represented activity mediated via the pontine nuclei. Dow (1949) also described long-lasting negative cerebellar potentials in response to local electrical stimulation of the cerebellar cortex in cats. He concluded that this potential was due to activity in the dendrites of the Purkinje cells.

Adrian (1943) studied the afterdischarges and the changes in spontaneous activity in the cerebellum following stimulation of the motor cortex in cats and monkeys. He found a localization within the anterior lobe and lobulus simplex corresponding to that described for the spino-cerebellar impulses (Snider and Stowell 1942, 1944). Stimulation of the hindleg motor area elicited responses in the contralateral lobulus centralis, the forelimb motor area in the culmen and the face area in the lobulus simplex.

Hampson (1949) extended this investigation stimulating face-, fore- and hindlimb sensory areas of the cerebral cortex of the cat, the localization of which had been determined in the same animals by means of evoked potentials. Stimulation of the subdivisions of the somatic sensory area I of the posterior sigmoid gyrus evoked potentials in the anterior lobe and the lobulus simplex. This projection was of the somato-topic type and coincided with that described by Snider and Stowell (1942, 1944) and by Adrian (1943) for peripheral impulses. Stimulation of the somatic sensory area II evoked potentials in the paramedian lobule. With precise threshold stimulation Hampson demonstrated a somato-topic localization in the paramedian lobule similar to that described by Snider and Stowell (1944) for the tactile system. The foreleg was represented in the more anterior folia and the hindleg in the posterior folia of the paramedian lobule. Hampson also found potentials in the ansiform lobule following stimulation of the so-called medial wall autonomic eyefield as outlined by Siebens and Woolsey (1946).

The findings of Hampson (1949) were to a great extent confirmed by Snider and Eldred (1951). They obtained the same distribution of responses in the cerebellum of cats whether the anterior sigmoid (motor) or posterior sigmoid (sensory somatic I) gyri were stimulated. From this area potentials were evoked in the anterior lobe as well as in the paramedian lobule. The localization of the forelimb-hindlimb responses corresponded to that described for the peripheral spinal impulses (Snider and Stowell 1942, 1944; Adrian 1943).

Snider and Eldred (1952) also reported responses in the ansiform lobule in monkeys following stimulation of cortical areas 4 and 6. Following stimulation of the somatic area II they obtained "conflicting data" which they did not discuss further (Snider and Eldred 1951, 1952).

It is of considerable interest that the somato-topic localization of the afferent impulses in the cerebellum (Snider and Stowell 1944; Adrian 1943; Hampson 1949) has also been observed with regard to the efferent projections from the same areas (Hampson, Harrison and Woolsey 1946, 1950; Nulsen, Black and Drake 1948).

Szabo and Albe-Fessard (1954) and Albe-Fessard and Szabo (1954) have recorded potentials in the paramedian lobule in response to stimulation of spinal nerves as well as the cerebral cortex. With regard to the spinal impulses they subdivided the paramedian lobule into three longitudinal zones, characterized by differences in latency and degree of interaction between impulses from different limbs. They also found a certain antero-posterior localization with the forelimbs represented in the anterior and the hindlimbs in the more posterior folia of the paramedian lobule. On stimulation of the somatic sensory area I and II and the motor area of the cerebral cortex they found no localization in the paramedian lobule and they describe no difference between the responses elicited from the different cortical areas.

The explanation of the differences with regard to the degree of localization in the cortico-cerebellar system found by Dow (1942) and Szabo and Albe-Fessard (1954) on the one hand and Hampson (1949) and Snider and Eldred (1951, 1952) on the other, is probably a question of the kind and the level of anaesthesia employed. Combs (1954) showed that this was the case, at least, for spinal impulses to the anterior lobe, and it is considered likely that the same is true for the cortico-cerebellar impulses.

(2) Anatomical studies

There exist a great number of anatomical investigations of the afferent connections to the cerebellar hemisphere. In the following only the more recent works of particular interest for the present study will be mentioned. For more complete refrences the reader is referred to the review of Jansen and Brodal (1954).

(a) *The cortico-ponto-cerebellar system* forms the largest afferent path-

way to the cerebellar hemispheres. Cortico-pontine fibres originate from the frontal as well as the parietal, occipital and temporal lobes (Mettler 1935a, b, c, d; Sunderland 1940; Nyby and Jansen 1951). In contrast to some early investigators, Nyby and Jansen arrived at the conclusion that the cortico-pontine fibres terminate in well defined longitudinal zones with comparatively little overlap. The fronto-pontine fibres originate in both the motor, premotor and prefrontal cortex and terminate in the medial and dorsal parts of the pontine nuclei. The parieto-pontine and occipito-pontine fibres terminate in the lateral part of the peduncular gray and in the lateral pontine nucleus. The temporo-pontine fibres are distributed to the dorsolateral pontine nucleus. The contribution of pontine fibres from the occipital and temporal lobes appears to be relatively modest in the monkey. The great majority of the cortico-pontine fibres project ipsilaterally, but a few also terminate on the contralateral side.

As regards the ponto-cerebellar projection Brodal and Jansen (1946) found in their experimental investigation in cats that the pontine fibres to the paraflocculus originate in two rather well defined areas, viz. one laterally in the lateral nucleus and the other rostrally in the paramedian nucleus. The ansoparamedian lobule receives its pontine fibres from the peduncular and lateral gray and from parts of the paramedian and ventral gray. The experiments reported did not permit the distinction of separate areas of origin for the fibres to the crus I, crus II and the paramedian lobule, respectively. The majority of the ponto-cerebellar fibres are crossed. Some ipsilateral fibres were found to project to the vermis and paraflocculus, but very few to the ansoparamedian lobule.

Based on the results of Brodal and Jansen (1946) and on their own investigation, Nyby and Jansen (1951) comment on the relation between the different parts of the cerebral cortex and the cerebellum. It was inferred from these studies that the frontal lobe projects to the vermis and to a lesser extent to the hemispheral parts of the corpus cerebelli. The temporal lobe apparently is related to the vermis, while the occipital and parietal lobes seem to project mainly on the ansoparamedian lobule. The paraflocculus receives the vast majority of its impulses from the parietal and occipital lobes. No experimental data seem to be available concerning possible differences in the origin of the afferent connections of the dorsal and ventral paraflocculus.

(b) *The inferior olivary complex* also contributes substantially to the afferent systems of the cerebellar hemispheres as is evident from Brodal's (1940) detailed analysis. The olivo-cerebellar projection is apparently predominantly contralateral and displays a high degree of point to point relationship. Each part of the cerebellum is related to a well defined area of the olive. Recently Walberg (1956) has published a detailed study of the origin and termination of the descending connections to the inferior olive. Like Mettler (1935 b, c) he found cortico-olivary connections, the fibres of which originate from all major cortical regions but with a considerable overweight from the sensory-motor cortex. The fibres terminate bilaterally in those parts of the inferior olive which, according to Brodal (1940), project to the paramedian lobule, crus II, the vermis of the posterior lobe and the lateral parts of the anterior lobe. Walberg found no difference in the terminal area for the fibres from the forelimb and hindlimb areas of the sensory-motor cortex. The same author, furthermore, describes strio-olivary fibres taking origin in the caudate nucleus and the globus pallidus. These fibres terminate bilaterally in those parts of the olive that project to crus I of the ansiform lobule and (caudate fibres) to the flocculo-nodular lobe (Brodal 1940). Mettler (1944) described the anulo-olivary tract originating in the periaquaeductal gray. This tract, supplemented by fibres from the red nucleus, proved in Walberg's experiments to be the richest source of descending fibres to the olive. The fibres from the periaquaeductal gray are distributed to that part of the olive which is related to the entire contralateral cerebellar hemisphere and vermis of the posterior lobe. The terminal area of the fibres from the red nucleus, however, was restricted to the olivary subdivision projecting to the crus I.

(c) As confirmed by Brodal (1943) *the lateral reticular nucleus* also sends fibres to the cerebellar hemisphere. The descending connections to this nucleus are, however, little known.

Since we are here concerned merely with the projection of cerebral impulses to the cerebellum, the spinal routes are left out of consideration.

The mode of termination of the afferent fibres in the cerebellar cortex still remains a controversial subject. Cajal (1911) described

two types of afferent cerebellar fibres, viz. climbing fibres terminating in relation to the Purkinje cells and mossy fibres terminating in relation to the granule cells. Cajal suggested that the climbing fibres originated in the pontine nuclei whereas other afferent systems terminated as mossy fibres. Lorente de Nó (1924), on the other hand, arrived at the conclusion that all afferent fibres to the cerebellum end as mossy fibres and that the climbing fibres represented recurrent collaterals of the Purkinje cells. A third conception was advocated by Jakob (1928), Strong (1929) and Strong and Elwyn (1943) who suggested that all the cerebellar afferent projection systems contributed both mossy and climbing fibres to the cerebellar cortex. Snider (1936) and Mettler and Lubin (1942) demonstrated that the pontine brachium terminated as mossy fibres. Carrea, Reissig and Mettler (1947), furthermore, showed that also the olivocerebellar fibres terminated as mossy fibres and they concluded that the climbing fibres presumably were derived from the cerebellar nuclei.

It seems strange, however, that all the climbing fibres should originate from the comparatively few cells of the cerebellar nuclei. Especially if, as maintained by Carpenter and Penny (1952), they are derived from the roof nuclei only, and not from the dentate nucleus. That the climbing fibres are recurrent collaterals of Purkinje cells is difficult to reconcile with the findings in pathological material with destruction of the majority of the Purkinje cells without changes in the climbing fibres (Cajal 1934; Mettler and Goss 1946).

Apparently it is more difficult to demonstrate degenerative changes in the climbing fibres than in the mossy fibres as also suggested by Brodal (1943). The possibility that some of the climbing fibres originate in one or more of the cerebellar relay nuclei cannot yet be completely ruled out.

Chapter II

Material and methods

Material. — The experiments presented were carried out in 114 adult cats (weight from 2 to 5 kg). On account of technical difficulties and the instability of the cerebellar evoked potentials a few of the experiments did not give positive results.

Anaesthesia. — The majority of the animals were anaesthetized with a combination of a barbiturate (Nembutal 15 mg/kg) and chloralose (30 mg/kg) administered intraperitoneally. The animals were maintained under light anaesthesia by additional injections of 0.1 ml (6 mg) of Nembutal when necessary. This anaesthesia proved to be satisfactory for recording of cerebellar action potentials. The level of anaesthesia during the recording was such that a flexor reflex could be elicited by pressing the toe pad of the animal. Whenever it was necessary to avoid muscular contractions due to the stimulation the animals were immobilized by intravenous decamethonium iodide (Decacurin AFI) 0.1 mg/kg, repeated whenever necessary. Simultaneously artificial respiration was carried out through a tracheal cannula with a vacuum-driven respirator. Pure oxygen was supplied under positive pressure (ca. 25 cm H_20). In order to study the distribution of cerebellar evoked potentials not depressed by barbiturate, a few experiments were carried out with chloralose (60 mg/kg) anaesthesia only and decamethonium immobilization.

Operative procedure. — The head of the animal was secured in a Horsley-Clarke stereotaxic instrument. The scalp was reflected and the neck muscles cut close to the skull. The bone overlying the posterior and lateral parts of the cerebellum was removed partly

with a dental burr and partly with a rongeur. The dura was split and part of the cerebellar hemisphere was exposed, care being taken not to disturb the pial circulation. In order to reach the anterior parts of crus I and paraflocculus, the occipital lobe was removed by suction and the tentorium was rongeured away.

The cerebral hemisphere was exposed by reflecting the temporal muscle and subsequent removal of the skull as described above. Better access to the somatic areas I and II was obtained by resection of the roof of the orbit. The orbital surface was exposed after removal of the zygomatic arc and the orbital contents. The cortex of the medial surface was reached after sucking away the opposite hemisphere. The tentorial surface of the hemisphere was exposed by gently lifting the occipital pole with a spatula.

Bleeding was controlled by bone wax and gelfoam. To prevent drying of the surface the exposed cortex was liberally irrigated with warm mineral oil or Ringer's solution (37° C). The temperature in the recording room was generally kept between 28° and 30° C.

The subcortical structures stimulated were reached by means of bipolar penetrating electrodes oriented according to the coordinates given by Gerard, Marshall and Saul (1936) and Jimenez-Castellanos (1949). The pons was stimulated from the ventral surface of the brain as well after cutting the trachea and oesophagus, removal of neck muscles and the basal cranium. The olive was stimulated by this ventral approach only.

The peripheral nerves stimulated in order to study the interaction between spinal and cortical impulses were the superficial radial and the sciatic nerve. They were dissected free and cut peripheral to the stimulating electrode.

Intravenous injections of decamethonium or anaesthetics were administered through the femoral or radial vein. For continuous injections a polyethylen-coated cannula was used.

Drugs were applied locally to the cerebellar cortex by means of a 2 × 2 mm filter paper soaked in the solution to be tested (strychnine nitrate 2–5 mg ml and novocaine 20 mg/ml). Surplus solution on the filter paper was carefully removed before application to the cerebellar cortex in order to minimize the spread of the drug to neighbouring regions.

The various subcortical lesions in the brain stem were produced by a small knife. Cortical cerebral and cerebellar areas were removed by subpial suction.

Stimulation was carried out with bipolar electrodes. Silver ball electrodes (200–300 μ) with an interpolar distance of 2 mm were used to stimulate the cortical surface. The subcortical structures were excited through two electrolytically pointed needles, isolated except for the tips (Grundfest, Sengstaken, Oettinger and Gurry 1950). The distance between the needle tips was about 1 mm. The electrodes were carried in an adjustable electrode holder allowing movements in steps of one mm in any direction.

A stimulator was used producing square wave pulses with independently controlled frequency, pulse duration and voltage. The parameters employed were single shocks with a repetition periode of $^1/_3$ sec., pulse duration 0.1 msec. and voltage up to 30 V. Generally supramaximal shocks were used. Threshold stimulation was used in experiments mapping finer differences between projection zones of neighbouring cortical areas. In studying the interaction between different impulses to the same cerebellar point a second similar stimulator was employed. The interval between the two stimuli could be varied from 0 to 500 msec.

In some experiments the foreleg and hindleg areas in the somatic sensory areas I and II were identified by stimulation of peripheral nerves and recording of the cortical evoked potentials. In the orbital gyrus the area giving inhibition of respiratory movements was identified by high frequency stimulation (cf. Kaada 1951).

Recording technique. — The cerebellar action potentials were recorded with different types of electrodes. In the mapping experiments bipolar stainless steel wire electrodes (diameter 0.2 mm, interpolar distance 1 mm) were employed in order to avoid recording distant electrical activity. The polarity of the potentials was checked with monopolar recording, the indifferent electrode being connected to the reflected skin flap. For studying the characteristics of the cerebellar potentials, the monopolar recording technique only was used.

In recording the electrical activity of the different layers of the cerebellar cortex and of the inaccessible parts of the ventral paraflocculus, electrolytically pointed stainless steel needles (Grundfest *et al.* 1950) with a tip diameter of 20–30 μ were employed. These electrodes were insulated, except for the tips. The insulation was checked before and after each experiment by testing bubble formation during weak electrolysis in saline under a microscope. The

penetrating electrodes were carried in a micro-manipulator allowing graded vertical movements of 0.01 mm.

The electrodes sometimes produced a "dimpling" of the cerebellar cortex before penetrating the pia. The electrodes were therefore retracted a little after each penetration. The activity in the various cortical layers was recorded and compared both on inserting and retracting the electrodes. The readings taken on the micro-manipulator were later compared with the extent of the electrode track as seen in the histological sections. Corrections were allowed for shrinkage during fixation.

The recording system consisted of a four-stage push-pull amplifier. An external cathode follower was connected between the recording electrodes and the amplifier input. The impulses were visualized on a cathode-ray oscilloscope with sweeps synchronized with the stimulus. To provide baseline stability the time constant of the recording system was usually 10 msec. The form of the recorded potentials was frequently checked by increasing the time constant to 70 or 200 msec. No significant change in the form of the potentials was observed on increasing the time constant.

Histological examinations. — At the end of the experiments the brain was removed and fixed in 10 per cent formalin. To study the extent of the experimental lesions in the brain stem and the cerebellum, the brains were cut in serial sections (20 μ) and every 25th section mounted and stained with thionine. To study the penetrating electrode tracks in the cerebellar cortex the brain was cut in sections of 10 μ thickness approximately parallel to the electrode tracks. Each 5th section was mounted and the sections were alternately stained with thionine and silver impregnated by the method of Nauta for better identification of the electrode tracks (see Andersen 1956).

Chapter III

Cortico-cerebellar evoked potentials

(A) Analysis of the cortico-cerebellar evoked potentials

(1) Experimental results

As previously described by several investigators (Curtis 1940; Dow 1942; Hampson 1949; Snider and Eldred 1951, 1952; Szabo and Albe-Fessard 1954) the cerebellar response to single shock stimulation of the cerebral cortex, recorded with a monopolar electrode on the cerebellar surface, usually consists of a positive deflection followed by a negative phase of smaller amplitude and longer duration. During the slow negative wave there is generally an increase in the spontaneous activity of the cerebellar cortex. The duration of the initial positive wave ranges from 10–30 msec., while the negative phase may last up to 100 msec. The form of this potential is quite similar to the cerebellar action potentials elicited by stimulation of other afferent sources (Dow 1939; Dow and Anderson 1942; Grundfest and Campbell 1942; Snider and Stowell 1944; Bremer and Bonnet 1951a; Bremer 1952; Bremer and Gernandt 1954; Carrea and Grundfest 1954; Combs 1954). It has not been possible, however, to differentiate in the cortico-cerebellar action potentials the early components corresponding to those called I and II by Carrea and Grundfest (1954).

According to their latencies, the cerebellar action potentials elicited by cerebral cortical stimulation may be divided into groups (fig. 1).

(1) *Short-latency potentials (2–6 msec.).* — The duration of the surface-positive wave varied from 20–30 msec., and the culmination time was 10–15 msec. (fig. 1, records B3, C4, and D4). Under the experimental conditions prevailing in these experiments the voltage of the short-latency potentials measured about 0.5 mV. The short-

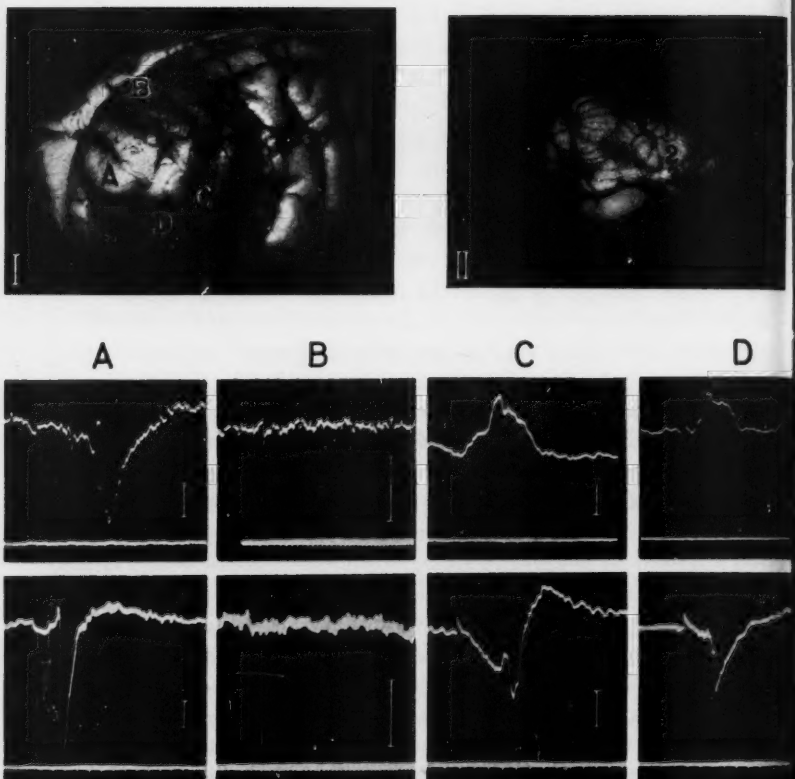


Fig. 1.

latency potentials were of constant amplitude and latency from sweep to sweep.

These potentials were most easily recorded from the paramedian lobule on stimulation of the anterior ectosylvian gyrus (fig. 1, record C4), but they may also be obtained by stimulation of parts of the lateral (fig. 1, record B3) and orbital gyri (fig. 1, record D4), and occasionally by stimulation of the most lateral parts of the anterior and posterior sigmoid gyri.

(2) *Long-latency potentials (12–25 msec.).* — These potentials have a very sharp initial positive deflection with a duration of 7–12 msec. (fig. 1, records A1–4). Recorded with surface electrodes the amplitude amounted to about 1 mV. The long-latency potentials were most typically recorded from the ansoparamedian lobule and the paraflocculus on stimulating the anterior sigmoid gyrus (fig. 1, records A1–4). In contrast to the short-latency response, the amplitude and latency of the long-latency response may vary considerably from sweep to sweep especially if the frequency of stimulation is higher than 1 per 3 sec. As the amplitude increases, the latency decreases. This variation in the amplitude-latency relationship sometimes occurred in periods of about 20–30 sec. without any correlation with the respiratory movements.

(3) *Combined short- and long-latency potentials.* — An apparent combination of the above-mentioned short- and long-latency potentials was frequently recorded in the ansoparamedian lobule on stimulating the anterior ectosylvian gyrus or the lateral parts of the anterior and posterior sigmoid gyri (fig. 1, records C2, D3). The latencies of the two components were about the same as the pure short- and long-latency potentials. The long-latency component often exhibited a similar variation in amplitude and latency as did the pure long-latency potential. The long-latency deflection might be completely absent from one or several sweeps and might recur at more or less definite intervals like the pure long-latency potentials.

Fig. 1. Types of potentials evoked in the contralateral cerebellar hemisphere (at points 1–4 in II) following stimulation of the cerebral cortex (points A–D in I). — (A) Anterior sigmoid, (B) anterior part of lateral, (C) anterior ectosylvian, and (D) orbital gyri. Corresponding records seen in columns A, B, C and D below. — (1) crus I, (2) crus II, (3) dorsal paraflocculus, (4) paramedian lobule. Corresponding records seen in lines 1, 2, 3, 4. Upward deflection indicates negativity at the "active" lead in this and all subsequent figures.

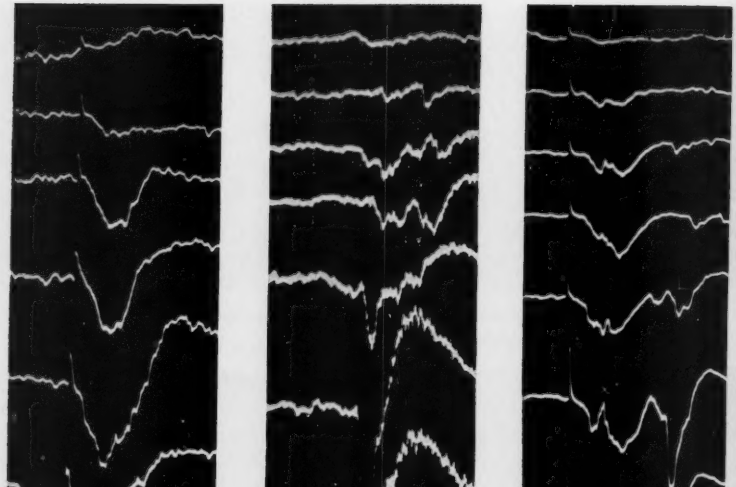


Fig. 2. Development of cerebellar evoked potentials on gradually increasing stimulus strength. — (A) Short-latency potential recorded in paramedian lobule following stimulation of the contralateral anterior ectosylvian gyrus. — (B) Long-latency potential in paramedian lobule in response to stimulation of the contralateral posterior sigmoid gyrus. — (C) Combined short- and long-latency potential evoked in crus II, from the anterior ectosylvian gyrus. Short- and long-latency components labelled S and L, respectively. Negative "spike" in the short-latency component indicated by x. Numerals below each record indicate stimulus strength in arbitrary units.

The development of the three types of responses on increasing stimulus strength is illustrated in fig. 2. As the records are taken from different experiments, the stimulus strengths which are given in arbitrary units below each record are not comparable between the three experiments. The absolute threshold of the response is greatly dependent upon the depth of anaesthesia, being considerably higher during deep anaesthesia. As is apparent from fig. 2, the latency of the responses decreases with increasing stimulus strength,

and the late negative wave appears first upon application of rather strong stimuli.

Column A in fig. 2 shows the development of a short-latency potential. Except for the last record the potential consists of a simple positive deflection and a late negative wave. In the last record the duration of the positive deflection is decreased and in addition there appears a rather sharp positive deflection superposed on the original positive wave. This sharp deflection apparently corresponds to the long-latency sharp deflections described below.

Fig. 2B shows the development of a long-latency potential. The responses to approximately treshold stimuli (records 14, 15 and 16) consist of solely long-latency, quite irregular activity. In the last record some short-latency activity is observed. This was frequently seen in the long-latency potentials on strong stimulation, as also observed by Dow (1942). The amplitude of this short-latency activity was always quite small.

The changes seen in a combined short- and long-latency potential on increasing stimulus strength are shown in fig. 2C. On record 28 the short-latency wave is labelled S and the long-latency deflection L. The two components have approximately the same threshold. There is a great variation in the latency and duration of the long-latency activity at threshold stimuli (records 22 and 25). With higher stimulus intensities the amplitude of the long-latency deflection increases rapidly.

In the potential shown in fig. 2C the short-latency positive wave is interrupted by a short negative deflection on the descending limb (indicated by X on record 33). This negative deflection is already present at threshold excitation. The time relations of this negative component conform with the negative spike observed following peripheral sensory stimulation as described by Bremer and Bonnet (1951a), Bremer and Gernandt (1954) and Widén (1955). It is apparently elicited more readily by auditory and other peripheral stimuli than from the cerebral cortex.

As mentioned by previous investigators (Dow 1939, 1942; Szabo and Albe-Fessard 1954; Combs 1954) *surface-negative action potentials* are often encountered in the cerebellum on stimulating various afferent pathways (fig. 1, records C1 and D1). In response to cerebral cortical stimulation this activity was either of the short-latency, or long-latency, or combined short- and long-latency type as described above for the surface-positive potentials. The voltage

of the surface-negative potentials was smaller than that of the positive ones. As also described by Dow (1942) a shift of the stimulation electrode to a neighbouring point in the cerebral cortex may completely reverse the sign of all components of the action potential from an identical cerebellar lead point (fig. 3). The initial negative action potential was recorded from all parts of the cerebellar hemisphere examined in the present study. Most frequently, however, it was found in crus I and the lateral part of crus II. In crus I the surface-negative action potentials were observed just as frequently as the positive ones.

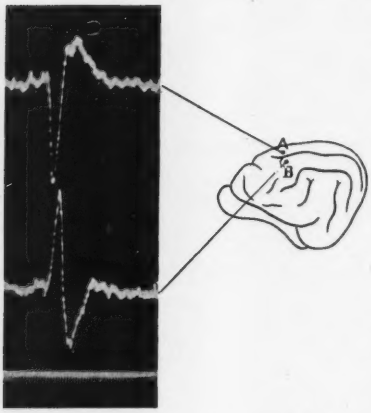


Fig. 3. Polarity change of potential in posterior part of the dorsal paraflocculus following a shift of the stimulating electrode from A to B.

Occasionally cerebellar action potentials were seen with a short-lasting initial negativity which was soon followed by the main positive short- or long-latency deflection (fig. 1, record A2). A corresponding short-lasting initial negativity has been described by Bohm (1953) and Widén (1955) in the spino-cerebellar action potentials. When the main positive deflection was blocked, for instance by postreactional subnormality, there was occasionally an apparent increase in this initial negativity (cf. fig. 36).

Records obtained from *different layers of cerebellar cortex* by a penetrating, sharp needle electrode (20 μ) exhibit characteristic changes. The records are often difficult to analyse on account of the instability of the baseline produced by the respiratory movements and the spontaneous variations in amplitude of the long-latency potential.

Fig. 4 shows an electrode track in the paramedian lobule and the form of the action potential recorded at indicated depths (0.1 mm apart). The top records from the molecular layer (M) consist of a pure long-latency potential with a considerable late negative, long-lasting deflection. As the Purkinje cell layer (P) was approached the positive potential decreases (records 2, 3, 4) and, corre-

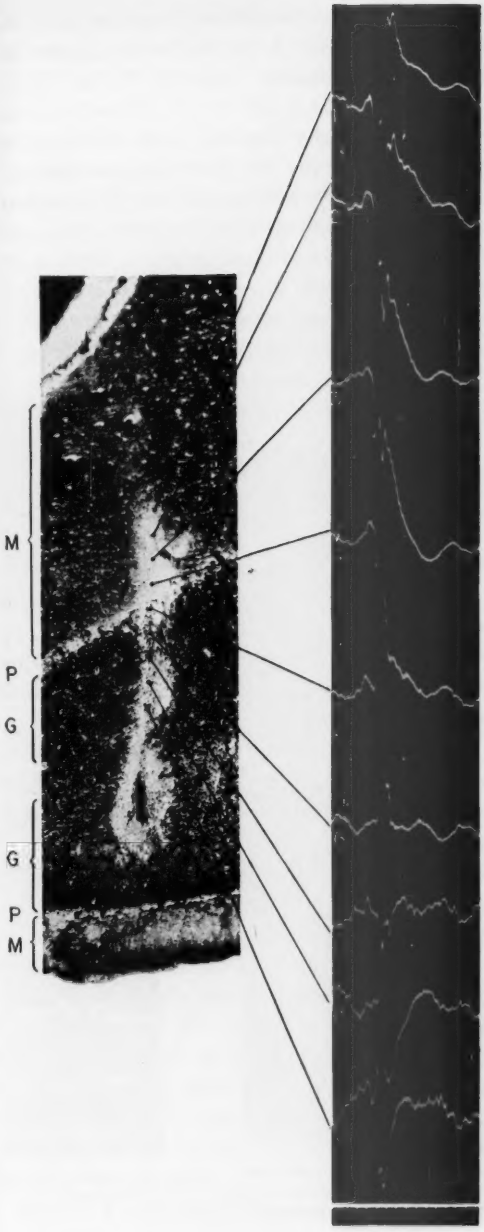


Fig. 4. Records (1–9) from different layers of the cortex of the paramedian lobule following stimulation of anterior sigmoid gyrus. Section showing electrode track. Records obtained at indicated depths (0.1 mm apart). M, molecular layer. P, Purkinje cell layer. G, granular layer.

sponding to this cell layer, a complete reversal of the polarity of the positive deflection took place (records 5, 6), indicating that the electrode has passed the active elements (Lorente de Nó 1947; Bishop 1949). The slow negative wave similarly seemed to reach an isopotential line corresponding to the Purkinje cell bodies or a little deeper (record 6). Still deeper the late wave reappeared but now as a positive deflection (record 8). The latency to the ascending phase of the surface-negative deflection was progressively increased as the surface of the molecular layer was approached (records 4, 3, 2). This suggests a slow conduction of the surface-negative wave towards the surface as will be discussed later.

The changes which take place in a combined short- and long-

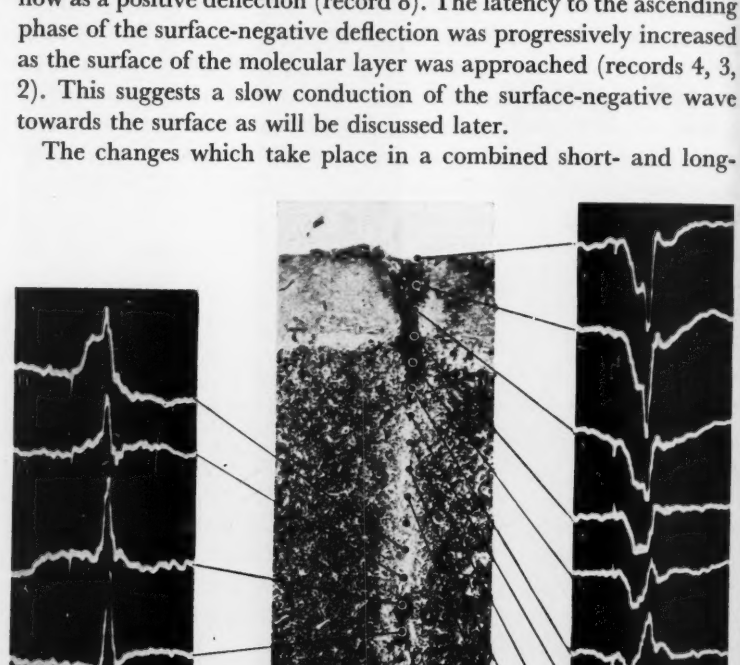


Fig. 5. Records (1–16) from different layers of the cortex of the paramedian lobule following stimulation of the posterior sigmoid gyrus. Section showing electrode track. Records obtained at indicated depths (0.1 mm apart).

latency potential at different depths in the cortex of the paramedian lobule are illustrated in fig. 5. The response from the molecular layer (records 1, 2, 3) exhibits the usual appearance of a double positive wave. As in fig. 4 the reversal of polarity of the long-latency deflection took place corresponding to the perikarya of the Purkinje cells (record 4). The reversal of polarity of the short-latency deflection occurred about 0.3 mm deeper, in the granular layer (records 7, 8). The records from the deeper part of the granular layer (records 9, 10) consist of a double negative wave not unlike the mirror image of the surface response.

Records 11–16 show the potential change as the electrode was moved through the next granular layer of the folded cortex without penetrating the corresponding Purkinje cell layer. Immediately below the perikarya of the Purkinje cells the record (16) consists of a short-latency positive component and a long-latency sharp negative deflection. The records (15–12) from different depths of this granular layer show a complete phase reversal of the short-latency component with little change of the long-latency negative component except for a decrease in amplitude as the electrode was moved from the Purkinje cells.

The polarity shift of the long-latency component was effectuated over a shorter distance than that of the short-latency component (fig. 5). This is consistent with the assumption that the long-latency component is due to activity in the Purkinje cells whereas the short-latency component represents activity in the granular layer which is comparatively thick and quite diffusely organized.

In order to determine other characteristics of the different types of cerebellar action potentials various drugs were applied to the cerebellar cortex at the recording point. The influence of asphyxia, the response to double shocks at varying intervals and the interaction between afferents from different sources were also investigated.

The effect of local application of strychnine was not quite constant in all experiments. As maintained by Bremer and Gernandt (1954) the concentration of strychnine applied is of great importance. In the present study rather weak strychnine solutions, from 0.1–0.5 per cent (1–5 mg/ml), were employed. Also the general responsiveness of the cerebellar cortex seemed to be of great importance for the effect of strychnine.

In fig. 6, column A, is shown an example in which the appli-

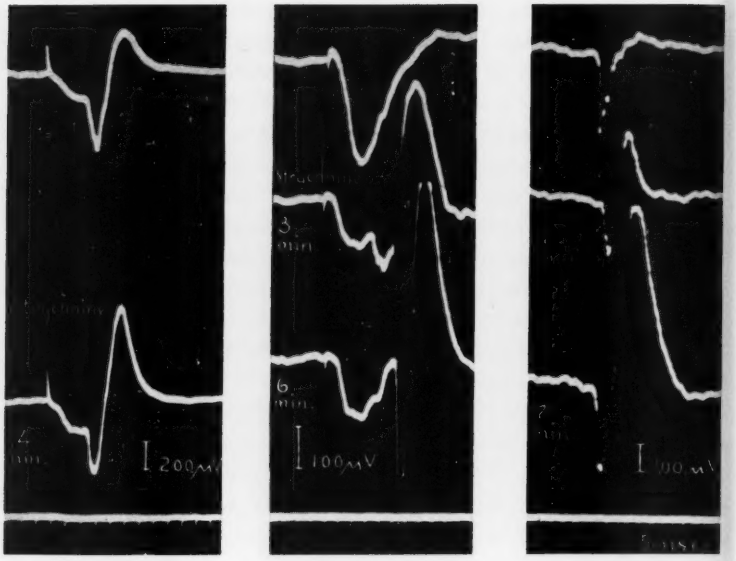


Fig. 6. Effect of local application of strychnine on cerebellar evoked potentials. All potentials recorded from the paramedian lobule following (A) stimulation of the anterior sigmoid gyrus, (B) anterior ectosylvian gyrus, and (C) anterior sigmoid gyrus. Top records, control; lower records taken at indicated intervals after strychnine application.

cation of strychnine greatly enhances the late negative wave, whereas the short- and long-latency positive components both remain practically unchanged. Column B demonstrates the changes in a short-latency potential following application of strychnine. From the records it is seen that while there was a decrease in the amplitude of the short-latency wave, there appeared a long-latency sharp positive deflection and at the same time there was a considerable increase in the late surface-negative wave. The long-latency potential in C was little influenced by strychnine, whereas again the late negative wave was greatly increased.

The enhancing effect of weak strychnine solutions upon cerebellar action potentials can be reversed by local application of a cortical depressant. Fig. 7 illustrates the depressant action of *novocaine* upon a combined short- and long-latency potential previously increased by strychnine. After 2 minutes of novocaine application the surface-negative wave was greatly reduced. Except for an incre-

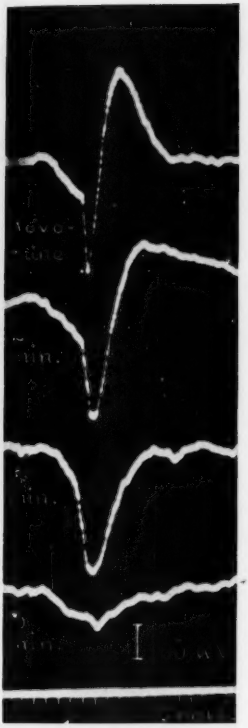


Fig. 7. Effect of 2 per cent novocaine on cerebellar evoked potentials recorded in the paramedian lobule in response to stimulation of the anterior sigmoid gyrus. Top record, control. Lower records taken 3, 5 and 10 min. after novocaine application.

ase in the duration, the two positive components were little affected. After 5 minutes all these changes were more evident. Not until 5 minutes later was a significant decrease in the amplitude of the short- and long-latency positive deflections observed. This effect of novocaine suggests that the late surface-negative wave originates in elements quite superficial in the cerebellar cortex or in elements especially susceptible to the depressant action of novocaine.

Asphyxiation had a differential action on the two positive components of the cerebellar evoked potentials (fig. 8). The three series of records are taken from different experiments. As is evident from the records, the long-latency component was less resistent and was completely blocked about one-half minute before the short-latency component, thus indicating their origin in different elements in the cerebellar cortex. The increase in the amplitude of the long-latency deflection just before the complete block of this component (column B, 3½ min.; column C, 4 min.) is perhaps due to the exciting effect of the increased CO_2 during asphyxiation (Gellhorn and Heymans 1948).

Fig. 9 demonstrates the effect of *paired stimuli of varying intervals* (indicated in msec. below each record) on the different types of cerebro-cerebellar evoked potentials. The short-latency potential in column A showed a slight depression only, as the stimulus interval was decreased. In column B a combined short- and long-latency potential is recorded. The long-latency deflection of the second response was greatly reduced at intervals of 50 and 43 msec. With still shorter intervals (35 msec.) the long-latency component reappeared and was again blocked at the shorter intervals (25 msec.). The short-latency deflection, on the other hand, remained quite

Fig. 8. Effect of asphyxia on cerebellar evoked potentials. Top records, control before asphyxiation. Duration of asphyxia indicated in minutes below each record. — (A) Stimulus I applied to the posterior sigmoid gyrus, stimulus II to the anterior ectosylvian gyrus. Recording from contralateral paramedian lobule. — (B) Response in the contralateral crus II to stimulation of anterior sigmoid gyrus. — (C) Bipolarly recorded response in the crus I on stimulation of anterior orbital gyrus. Bottom records, recovery after resumption of artificial respiration.

Fig. 9. Effect of double shock stimulation with varying intervals on the corticocerebellar evoked potentials. All records from contralateral paramedian lobule. Top records showing the unconditioned response to the second stimulus. — (A) Short-latency potential on stimulation of the anterior ectosylvian gyrus. — (B) Combined short- and long-latency potential in response to stimulation of the anterior sigmoid gyrus. — (C) Long-latency potential to stimulation of the posterior sigmoid gyrus. Shock intervals in msec. below each record.

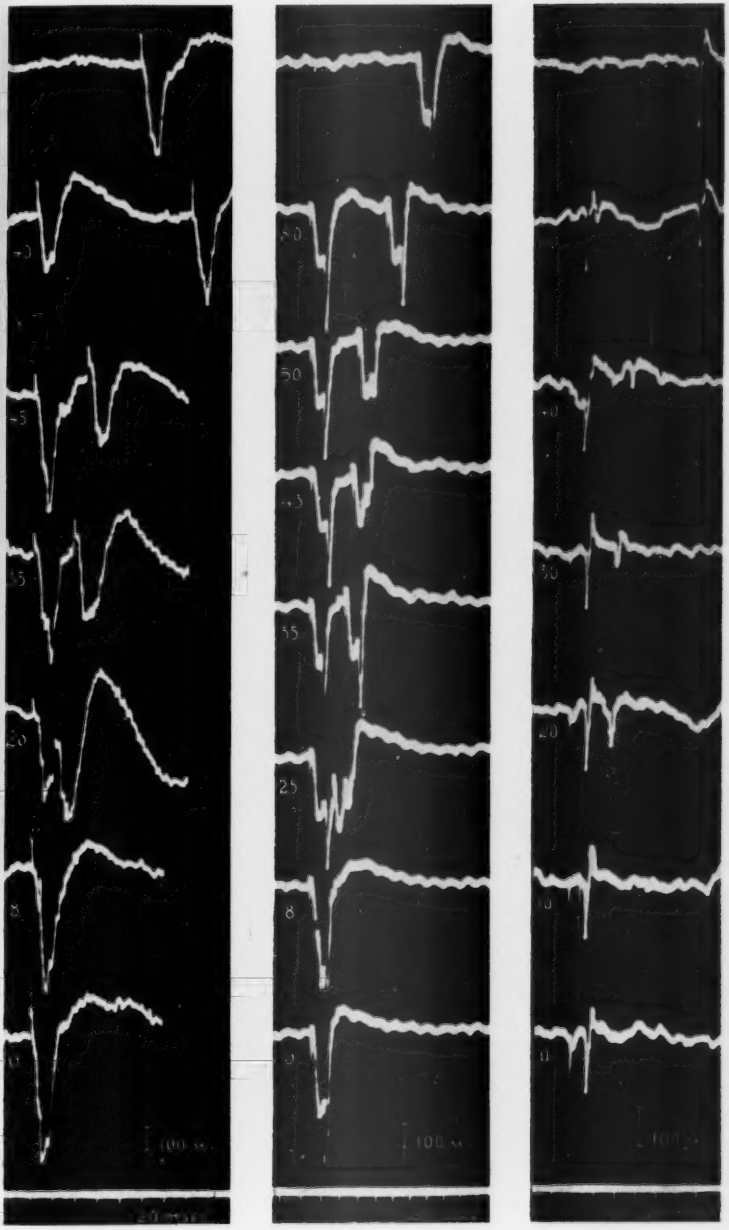


Fig. 9.

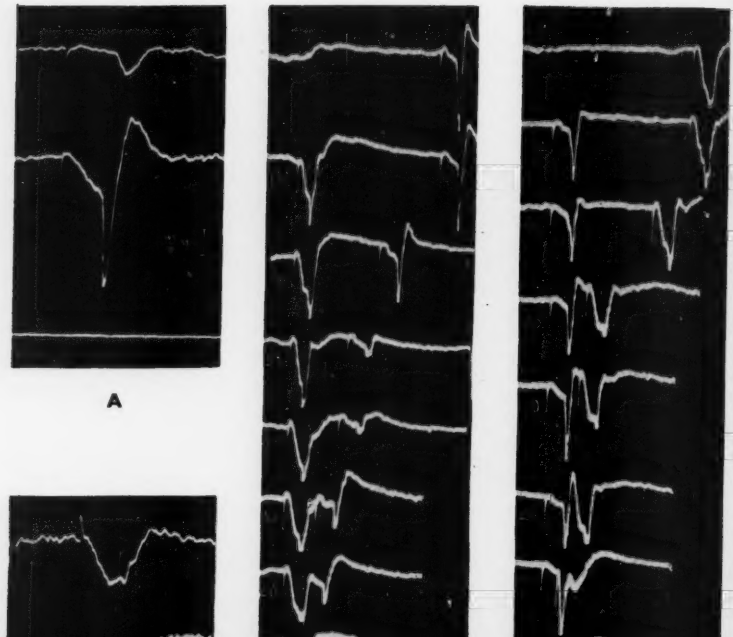


Fig. 10. Interaction in the paramedian lobule between a short-latency and a long-latency response. — (A) Long-latency response elicited from anterior sigmoid gyrus. — (B) Short-latency response at the same paramedian point to anterior ectosylvian stimulation. Stimulus strength indicated in arbitrary units below each record in A and B. — (C) Same short-latency potential as in (B) conditioning response; same long-latency potential as in (A) test response. — (D) Same potentials as in (C) but in reversed sequence. Intervals between conditioning and test stimuli in msec. below each record in (C) and (D).

unaffected except at the shortest intervals. A recovery cycle quite comparable to that of the long-latency deflection was obtained by Albe-Fessard and Szabo (1954) studying the interaction between cortical and spinal, or different spinal, impulses to the paramedian lobule. Stimulating the same spinal nerve with double shocks they never found a reappearance of the test response with the shorter intervals.

The long-lasting, late surface-negative wave of the test response in this experiment is also of considerable interest (fig. 9, column B). Compared to the unconditioned response the ascending limb of the negative deflection was steeper except at the shortest intervals (8 msec.). The amplitude of the surface-negative wave varied independently of the positive deflections. There was a definite increase in the negative wave at intervals less than 43 msec. The pure long-latency response (column C) had a recovery cycle quite comparable to that of the long-latency deflection of column B.

The experiments with double shocks have demonstrated further differences between the short- and the long-latency components of the cortico-cerebellar evoked potentials, the former showing very little poststimulatory subnormality. The summation of the surface-negative slow wave at short intervals is in agreement with the observations of Bremer and Bonnet (1951 a) on auditory potentials in the cerebellum.

A study of *the interaction between different afferents* converging upon the same cerebellar point has also provided some information about the origin and characteristics of the cerebellar evoked potentials. Fig. 10 A shows a long-latency potential with some short-latency activity (cf. fig. 2 B), and in column B a short-latency potential both recorded from the same point. Column C demonstrates that this short-latency potential had a pronounced conditioning effect upon the long-latency response. The test response was almost completely blocked at intervals of 55 and 45 msec. At intervals of 30 and 20 msec. there was some increase in the amplitude of the test response. At 12 msec. it was again completely blocked. The short-latency potential, on the other hand, was influenced only to a very small extent by a conditioning long-latency potential (fig. 10 D). The test response was practically unchanged until the interval was less than 15 msec.

The short- and long-latency positive deflections of the cortico-cerebellar evoked potentials are also conditioned differently by a

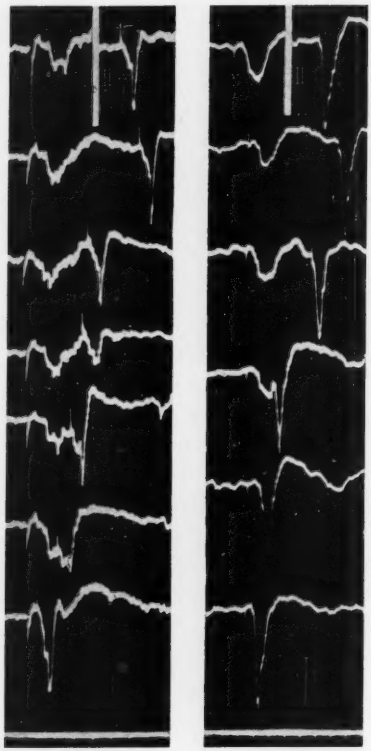


Fig. 11. Interaction between spinal and cerebral impulses recorded from the paramedian lobule. Conditioning response (I) in (A) and (B) evoked by stimulation of the ipsilateral superficial radial nerve. — Test response (II) elicited from contralateral anterior sigmoid gyrus (A), and from contralateral anterior ectosylvian gyrus (B). Intervals between conditioning and test stimuli in msec. below each record.

shock to a spinal nerve. In fig. 11A the test response (II) is of the long-latency variety with some short-latency activity (cf. fig. 2B). The records were obtained from the paramedian lobule. The long-latency deflection of the test response was completely blocked at a 55 msec. interval. At shorter intervals there was a transient increase of the test response. At a 30 msec. interval, however, the long-latency deflection was again blocked. In column B, on the other hand, the test response (II) is a short-latency potential. This shows comparatively little depression as the stimulus interval is shortened. At a 40 msec. interval there is a definite decrease in the duration of the test response, suggesting blocking of elements responsible for the later part of the short-latency deflection.

If the conditioning stimulation is applied to the cerebral cortex and the test stimulus to a peripheral nerve, the short- and long-latency potentials both have a long-lasting (50–60 msec.) depressing effect upon the spinal afferent impulses to the paramedian lobule.

As also described by Curtis (1940) some very late activity is sometimes seen in the cerebellum following single-shock stimulation of the cerebral cortex. The latency of this late activity may vary between 100 and 200 msec. (fig. 12A). The polarity of this potential is generally the same as that of the initial deflection. As maintained by Dow (1942) the potential occurs only rarely and its interpreta-

tion is therefore difficult. The "Curtis response" is frequently absent after a single cortical shock, but may appear after double shocks provided the interval between the two stimuli is not too short (fig. 12B). It is interesting that the "Curtis response" may have a well developed late negative wave (fig. 12A, top record). It is also remarkable that the minimum interval between repeated shocks capable of eliciting the "Curtis response" corresponds quite closely to that at which the long-latency positive component of the cerebellar response is blocked (fig. 12B).

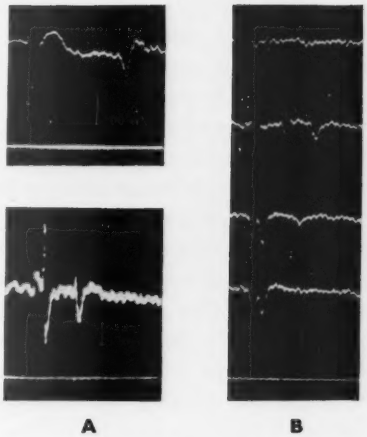


Fig. 12. Very long-latency activity in the cerebellum following stimulation of contralateral cerebral cortex. — (A) Upper record, potential from paramedian lobule following anterior ectosylvian stimulation. Lower record, stimulation of the anterior limbic gyrus and recording with a bipolar electrode in crus II. — (B) Double shock stimulation of the anterior sigmoid gyrus; record from the paramedian lobule. Upper record control with a single shock to the same point.

(2) Discussion

Comparatively few attempts have been made to analyse the evoked potentials in the cerebellum with regard to their origin in different elements of the cerebellar cortex. This is quite surprising as the histology of the cortex is uniform all over the organ and the most important features of the intracortical fibre connections seem to be quite well known (Cajal 1911; Scheibel and Scheibel 1954). The structure of the cerebellar cortex with all the Purkinje cells uniformly oriented in a single cell layer should prove favourable for the identification of the various components of the cerebellar potentials.

The first systematic description of cerebellar evoked potentials was made by Dow (1939). Based on the effects of asphyxiation of the animal, he concluded that the action potentials were due to activity in the cerebellar neurons and not in the afferent fibres. Dow (1949) in an important paper also described long-lasting negative potentials which he attributed to the dendrites of the Purkinje cells.

Stimulating spinal afferents to the cerebellum, Grundfest and

Campbell (1942) and Carrea and Grundfest (1954) distinguished three different components in the cerebellar response. The first of these was due to activity in the afferent fibres. The second was attributed to activity in the granular layer. This potential was generally surface-positive, of quite small voltage, and lasted about 6 msec. The third and largest component they described as due to complex intracerebellar activity. In the cerebellar potentials elicited from the cerebral cortex no separate, early activity attributable to incoming fibres was observed in the present study.

Bremer and collaborators (Bremer and Bonnet 1951a, 1953; Bremer 1952; Bremer and Gernandt 1954) made an extensive analysis of the cerebellar responses evoked by auditory and spinal stimulation and also of the strychnine convulsive pattern of the cerebellum by means of penetrating electrodes, asphyxiation and local application of strychnine and Nembutal. They desribe the general cerebellar evoked potential as a surface-positive deflection often interrupted by a sharp surface-negative spike and followed by a slow negative wave of smaller amplitude. As to the interpretation of the different components of this response, Bremer and Bonnet (1951a, 1953) conclude that the initial surface-positive phase represents activity in the cerebellar interneurons in the granular layer. The surface-negative spike represents a synchronized discharge of Purkinje cells, and the late surface-negative wave corresponds to an asynchronous after-discharge of the same cells. Bremer and Gernandt (1954) state that the initial positive deflection resists all local injuries including thermocoagulation and must therefore be a fibre potential.

Buser and Rougeul (1954) have analysed the cerebellar response to optical stimulation and Albe-Fessard and Szabo (1955) the response to spinal and cortical stimulation by means of intracellular records from Purkinje cells. They conclude that the positive surface responses* correspond to activity in certain elements of the Purkinje cell. They state further that the dendrites probably take part in this activity.

In attempting to interpret the cortico-cerebellar evoked potentials described in the preceding section it is natural to make a comparison with the evoked potentials of the cerebral cortex which have been quite extensively studied and which generally also consist of a surface-positive deflection succeeded by a long-lasting surface-negative wave.

The short-latency surface-positive deflection of the cortico-cere-

* It appears from their records that their positive surface responses to cortical stimulation are the long-latency potentials in the present study.

bellar potentials presumably represents activity in the granular layer due to the reversal of polarity of the potential in that particular region (fig. 5) (Bishop 1949). Like the surface-positive component of the primary cerebral cortical response it is probably some kind of post-synaptic cell potential (Bremer and Bonnet 1949; Bishop 1949; Chang and Kaada 1950; Amassian 1953; Cragg 1954; Albe-Fessard and Buser 1955; Perl and Whitlock 1955; Li, Cullen and Jasper 1956). The interpretation of the short-latency positive wave as due to activity in the granular cells is not incompatible with the suggestion of Grundfest and coworkers (Grundfest and Campbell 1942; Carrea and Grundfest 1954) that their potential II represents activity in the granular layer. Now, of course it is possible that the early part of this short-latency potential to some extent is due to activity also in the presynaptic terminals and the late part of it may represent activity set up at the termination of granule cell axons in the molecular layer. Indeed, the experiment shown in fig. 11 B suggests a multiple origin of the short-latency potential. At an interval between conditioning and test shock of 40 msec. there is a great reduction of the *duration* of the test response, indicating blocking of elements responsible for the later part of the short-latency potential.

The long-latency sharp positive component of the cerebellar response to cortical stimulation originates in other elements than the short-latency response as shown by the differences in interaction and resistance to asphyxia. Recorded with a penetrating electrode this component changes polarity very close to the perikarya of the Purkinje cells (fig. 4). Some experiments, in which the penetrating electrode has passed almost parallel to the layer of Purkinje cell perikarya, indicate that the reversal of polarity of the long-latency potential takes place slightly superficial to the Purkinje cell bodies. This means that the perikarya and the proximal parts of the dendrites act as a sink, whereas the peripheral parts act as a source for this potential. This again suggests that the long-latency surface-positive deflection of the cerebro-cerebellar evoked potentials is due to activity in the perikarya and proximal dendrites of the Purkinje cells (cf. Lorente de Nó 1947, 1952; Bishop 1949). This conclusion seems to be quite in agreement with those of Buser and Rougeul (1954) and Albe-Fessard and Szabo (1955) mentioned above. It is also consistent with the interpretation of the antidromic pyramidal response in the cerebral cortex given by Landau (1956) who attri-

buted the positive phase of the potential to activity in the perikarya and proximal dendrites of the pyramidal cells.

Regarding the interpretation of the slow surface-negative wave in the cerebral cortex there seem to be general agreement that it represents activity conducted towards the surface over the apical dendrites of the pyramidal cells (Chang and Kaada 1950; Bishop and Clare 1952; Bremer 1952; Tasaki, Polley and Orrego 1954; Li, Cullen and Jasper 1956). In the cerebellar cortex the Purkinje cell dendrites extending through the molecular layer to the surface can, to a certain extent, be regarded as analogous elements. The experimental data presented above demonstrate that the slow surface-negative wave of the cerebellar evoked potential originates in elements superficial in the cortex (fig. 7). The porarity of the surface-negative wave changes corresponding to the perikarya of the Purkinje cells (fig. 4). The wave appears progressively earlier as the Purkinje cell bodies are approached (fig. 4). These observations favour the suggestion that the slow surface-negative potential of the cerebellar response is due to activity conducted by the Purkinje cel dendrites toward the surface. This also seems to fit well with Dow's (1949) description of Purkinje cell dendritic potentials evoked by local stimulation of the cerebellar cortex.

On account of the small amplitude and instability of the surface-negative wave, a closer analysis of this component is as a rule difficult. If, however, the latency to the ascending phase of the surface-negative wave in fig. 4 is measured through the molecular layer, the estimated velocity of conduction of the surface negative wave is about 0.05 m/sec. This is a value much smaller than usually given for conduction along dendrites (Lorente de Nó 1947, 1952; Chang 1951 a, 1955; Cragg and Hamlyn 1955). There is a far better correspondence with the result of Buser (1956) who finds a speed of propagation along dendrites in the optic lobe of about 0.02 m/sec.

As in the cerebral cortex, the effect of local application of strychnine on the cerebellar evoked potentials is most pronounced and constant on the slow surface-negative wave which shows a considerable increase. In the cerebellar potentials evoked from the cerebral cortex no appearance of a surface-negative spike, as described by Bremer and Bonnet (1951 a), has been observed. The effect of strychnine on the short-latency positive deflection of the cerebellar responses has always been purely depressive (fig. 6B).

This depression cannot be explained as an effect of the great increase in the late surface-negative wave (Bremer and Stoupel 1956); it must be due to a depression of the elements responsible for the short-latency positive deflection. At the same time a sharp surface-positive deflection appears which rapidly increases in size as does the slow negative wave. It looks as if strychnine has a differential action on the various types of cells in the cerebellar cortex. This is not in agreement with Bremer and Bonnet (1953) who showed that after intravenous injection of strychnine there is an increase also of the positive component of the anterior lobe response to stimulation of the ipsilateral forefoot. It is difficult to exclude in their experiments (with int avenous strychnine) that the increase in the positive wave is due to facilitation for instance at the spinal synapses. The depressing action of strychnine on the short-latency positive potential may be due to a depression of the synaptic function of the cerebellar cells similar to that described for cortical cells by Chang (1953). However, the records of fig. 6B apparently are not consistent with Chang's view (1953) that strychnine does not increase the excitability level of individual neurons. In the records taken after 3 and 6 minutes of strychninization, a completely new set of neurons seem to discharge giving origin to the long-latency surface-positive deflection. If, on the other hand, the long-latency positive wave is well developed before the application of strychnine, it seems to be very little influenced by this agent (fig. 6A, C).

The effect of double shock stimulation on the evoked potentials of the cerebellar cortex was first studied by Dow (1939, 1942). He described a long-lasting depression (up to one second) of the long-latency potentials following cortical stimulation. In addition, the present study demonstrates short-latency potentials which show comparatively little postreactional depression and, furthermore, that the long-latency responses frequently reappear at shock intervals between 15 and 35 msec. (fig. 9). This may be a phenomenon corresponding to that described by Albe-Fessard and Szabo (1954) for the interaction between cortical and spinal, and different spinal, impulses. With double shock *cortical* stimitulation is difficult to exclude the possibility of local recruitment of cortical cells around the stimulated point at the shorter intervals. However, the investigation of the excitability changes of the cerebral cortex by Chang (1951 b) makes that possibility appear less likely. This author never

observed supernormality of the cerebral cortex following direct electrical stimulation. The similarity in time-relations between the interaction observed by Albe-Fessard and Szabo (1954) and the blocking of the second response to cortical stimulation favours the assumption that we are dealing with a cerebellar phenomenon. The available data do not definitely rule out the possibility, however, that it is due to the properties of the precerebellar nuclei, known to receive both cortical and spinal impulses (pons, inferior olive, lateral reticular nucleus (?)). A possible explanation of the reappearance of the second response is that suggested by Albe-Fessard and Szabo (1954) for their interaction curves. The first stimulus sets up a "subliminar fringe" around the activated neurons. The cells in this "subliminar fringe" are recruited at short stimulus intervals and thus the second response reappears during the increased excitability of the cells in the "subliminar fringe". The reason why Albe-Fessard and Szabo (1954) did not observe this phenomenon following double shock stimulation of spinal nerves may be that the second impulse was already blocked in the spinal cord on account of long unresponsiveness (Hughes and Gasser 1934).

The interaction between different afferent impulses (spinal, auditory, trigeminal) in the cerebellar cortex has been studied by Bremer and Bonnet (1951 b). They conclude that this interaction may be "une propriété générale de l'écorce cérébelleuse". In the present study interaction between different impulses to the same point has also been observed, but the interaction is quite different in degree and time relations for the various types of afferent impulses (short- and long-latency potentials and spinal impulses). Long-latency responses are depressed for up to 100 msec. following a short-latency conditioning impulse. The maximal depression is observed between 40 and 60 msec. The blocking effect of the short-latency responses is presumably set up by the granule cell axons acting on the Purkinje cell dendrites. At intervals below 40 msec. the long-latency test response frequently reappears. The explanation for this may be the same as that given for the effect of double shock stimulation of the cerebral cortex.

The short-latency potential is very little depressed by a preceding long-latency potential. At short intervals, however, a definite depression is observed which is difficult to explain (fig. 10D, intervals 15 and 8 msec.). It may possibly be due to the presence of some short-latency activity in the long-latency conditioning response (fig.

10A, fig. 2A). This depression has not been observed when two short-latency responses are recorded at corresponding intervals.

A definite conclusion as to where the observed interaction takes place is not possible from the present study. Experiments planned with a simultaneous recording of the responses to cortical stimulation both from the precerebellar nuclei (pons and inferior olive) and from the cerebellar cortex and white matter may throw some light on this question. The histology of the cerebellar cortex, however, is not incompatible with the assumption hat the interaction takes place at this level. The postulation that granule cell responses have a long-lasting depressing influence on the Purkinje cells through the granule cell axons, and that the Purkinje cell response has comparatively little influence on the granule cell activity, is in accordance with the experimental results presented.

The responses with very long latencies (100–200 msec.) first described by Curtis (1940) have not been studied systematically in the present investigation. Their inconstant appearance makes a closer analysis difficult. The observation made in fig. 12B suggests that they are dependent on Purkinje cell discharges. Perhaps they represent activity in a reverberating circuit corresponding to that suggested by Chang (1950) for the cortico-thalamic system.

(B) Distribution of evoked potentials in the cerebellar hemispheres

(1) Experimental results

As mentioned in chapter III A and indicated in fig. 1, stimulation of different parts of the cerebral cortex with single shocks in anaesthetized cats evokes activity in the cerebellar hemispheres, varying to some extent from area to area. While stimulation of some regions, as for instance the motor cortex, seems to activate the major part of the contralateral cerebellar hemisphere, only very limited portions of the cerebellar cortex are activated on stimulation of other parts of the cerebral cortex, such as for instance the anterior part of the lateral gyrus.

In the following a description and some maps will be presented showing cerebro-cerebellar relations as revealed by the evoked potential technique. It is inevitable that maps of this kind, presen-

ting the results of a series of experiments, must be somewhat schematic and in some ways misleading. Thus, the boundaries between the different areas are not as sharp as the diagrams may indicate. There is a considerable overlap on the neighbouring folia, and there is, furthermore, considerable variation from animal to animal in the distribution of the potentials, probably depending upon the level of anaesthesia and the general condition of the animal. The maps presented tend to indicate the maximum extent of excitable cerebral cortex with regard to the different cerebellar areas in lightly Nembutal and chloralose anaesthetized animals. In the last part of this chapter the distribution of potentials in the paramedian lobule in only chloralose anaesthetized animals will be described.

In the maps (figs. 13–21) the open circles indicate long-latency and crosses short-latency potentials. Crosses within the circle represent the combined short- and long-latency potentials; horizontal lines indicate regions yielding no responses in the particular cerebellar area tested.

(a) Dorsal paraflocculus

(i) *Posterior half of the dorsal paraflocculus.* — Under the conditions prevailing in the present experiments the posterior part of the dorsal paraflocculus in cat was activated on stimulating certain well limited areas of the cerebral cortex only, as is indicated in fig. 13. The potentials were most readily elicited from the contralateral anterior sigmoid gyrus (fig. 1, record A3). In lightly anaesthetized animals the excitable area extended over a considerable part of this gyrus, whereas in deeper anaesthesia the response could be elicited from a very restricted area close to the presylvian sulcus only. The recorded response was a typical long-latency potential (15–25 msec.)

Fig. 13. (A) Nomenclature employed in the present study. Abbreviations: an — ansate sulcus; B — olfactory bulb; cr — cruciate sulcus; EA — anterior ectosylvian gyrus; L — limbic gyrus; Lat — lateral gyrus; lob.p.m. — paramedian lobule; Or — orbital gyrus; P — proreate gyrus; pfl.d. — dorsal paraflocculus; pfl.v. — ventral paraflocculus; pr — presylvian sulcus; SA — anterior sylvian gyrus; SiA — anterior sigmoid gyrus; SiP — posterior sigmoid gyrus; SSA — anterior suprasylvian gyrus; SSM — middle suprasylvian gyrus.

(B) Cerebral cortical areas from which responses were elicited in the posterior part of the dorsal paraflocculus. Responsive area, black in the schematic drawing of the cerebellar surface. Symbols: cortical areas from which long-latency (o), short-latency (+), combined short- and long-latency (⊕), and no (—) potentials were evoked in the black paraflocculus area. The same symbols have been used in the subsequent schematic maps.

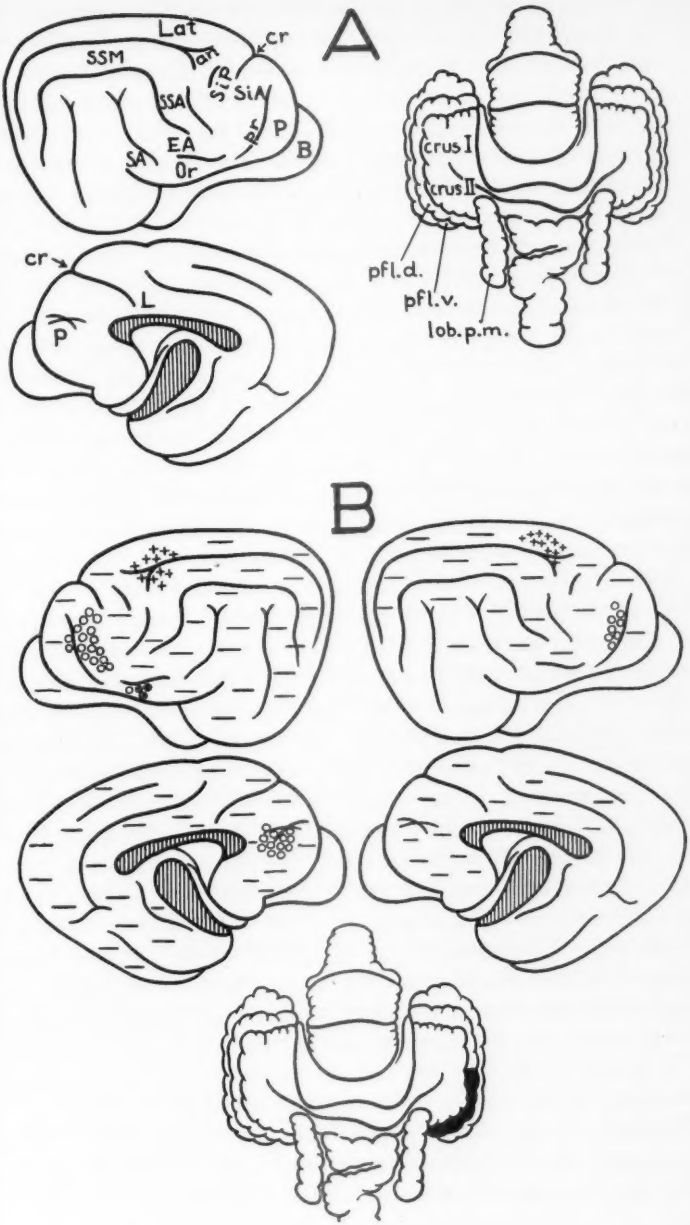

A
Lat
SSM
cr
SSA
SiA
EA
SA
Or
P
B
crus I
crus II
pfl.d.
pfl.v.
lob.p.m.
cr
P
L
B

Fig. 13.

as described in the preceding section. As a rule the amplitude was rather small, presumably due to the greater trauma and bleeding caused by exposure of the paraflocculus as compared with, for instance, exposure of the paramedian lobule. The potential was found in the seven or eight posterior folia of the dorsal paraflocculus. In general the amplitude was greatest in records from the 3rd or 4th folium no matter which point was stimulated within the effective sigmoid zone.

Stimulation of the area under consideration also elicited potentials in the paramedian and ansiform lobules (see below). The possibility that the parafloccular response was due to intracortical spread in the cerebellum has been ruled out by sucking away the paramedian lobule and the crus II. As a rule this procedure reduced the amplitude of the parafloccular response, but otherwise left the potentials intact. The fact that the potentials evoked in the crus II of the ansiform lobule by stimulation of the same cortical area are located in the medial part of the lobule and not in the lateral part likewise favours the assumption that we are dealing with a direct parafloccular response to afferent impulses.

Stimulation of a limited area in the anterior part of the contralateral lateral gyrus also evoked potentials in the posterior part of the dorsal paraflocculus (fig. 13). The greatest responses were usually found in the 2nd or 3rd folium from behind following stimulation of points about 10 mm behind the anterior end and about 5 mm medial to the lateral sulcus. In the neighbouring folia potentials with a smaller amplitude and a somewhat longer latency were often encountered. In very lightly anaesthetized animals the excitable area extended more laterally into the anterior suprasylvian gyrus. The potentials elicited from this parietal zone were of the short-latency type (about 6 msec.) described above (fig. 1, record B3). Moving the stimulating electrode a few millimetres sometimes resulted in a complete change of polarity of the parafloccular response (fig. 3). This may possibly signify that different parts of the small excitable zone in the anterior lateral gyrus may activate different neurons of the parafloccular cortex.

Stimulation of the same area of the lateral gyrus also evoked potentials in the anterior part of the paramedian lobule and less frequently in the medial part of the crus II (see below). These potentials were as a rule characterized by a smaller amplitude than was the parafloccular response, and in more deeply anaesthetized

animals the posterior part of the dorsal paraflocculus was the only cerebellar zone that could be activated from the lateral gyrus. It is unlikely, therefore, that this parafloccular response is due to intracortical cerebellar spread of activity.

In some experiments parafloccular action potentials were observed following stimulation of points in the anterior part of the contralateral orbital gyrus. It was shown that the area coincides with that yielding inhibition of respiratory movements (for references cf. Kaada 1951). The parafloccular potentials elicited from this region were of the long-latency variety or of the combined short- and long-latency type (fig. 1, record D3). The amplitude of these potentials was rather small and in most experiments they were difficult to obtain.

On stimulating the medial surface of the contralateral hemisphere a typical long-latency potential (12–20 msec.) was elicited in the posterior part of the dorsal paraflocculus. The excitable area (fig. 13) was a rather limited portion of the anterior limbic and proreate gyri. The threshold of this response was generally higher than that elicited in the same cerebellar area on stimulating the zones on the lateral surface of the cerebral cortex. This may be due to traumatization involved in sucking away the contralateral hemisphere to obtain access to the medial surface. It is difficult, however, to eliminate the possibility of spread of the stimulating current to the fibres from the anterior sigmoid gyrus running beneath the medial surface of the hemisphere. The lack of response in the paramedian lobule following stimulation of this part of the medial surface renders this possibility rather unlikely.

Stimulation of the ipsilateral hemisphere also elicited potentials in the posterior part of the dorsal paraflocculus. Generally the excitable ipsilateral zones coincided with those of the contralateral hemisphere, but were less extensive (fig. 13). The ipsilateral potentials conformed with the contralateral ones although the amplitude was smaller and the latency a little longer. Attempts to elicit parafloccular responses from the ipsilateral orbital and medial surfaces have been unsuccessful.

(ii) *Anterior part of the dorsal paraflocculus.* — From this area short-latency surface-positive potentials of low amplitude were recorded on stimulating part of the contralateral middle suprasylvian gyrus (fig. 14). Attempts to demonstrate a continuity between this area

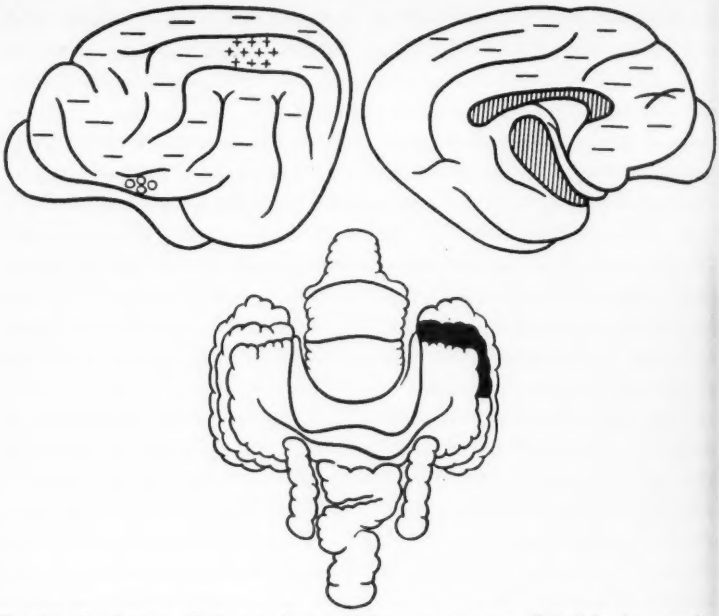


Fig. 14. Cerebral cortical areas from which responses were elicited in the anterior part of the dorsal paraflocculus. Symbols as in fig. 13.

and that of the anterior lateral gyrus giving potentials in the posterior half of the dorsal paraflocculus (fig. 13) were unsuccessful. In one experiment a long-latency potential was also picked up from the anterior part of the dorsal paraflocculus following stimulation of the anterior part of the orbital gyrus. The potentials in the anterior part of the dorsal paraflocculus were frequently absent and always of small amplitude, possibly due to the rather extensive operative procedure in these experiments.

Stimulation of the cortical areas investigated, other than those mentioned above, did not evoke action potentials in the dorsal paraflocculus.

(b) Ventral paraflocculus

The ventral paraflocculus proved very difficult to expose from the dorsal as well as from the ventral surface of the brain owing to excessive bleeding. Therefore, all the records from this lobule were obtained by means of a sharp needle electrode inserted through

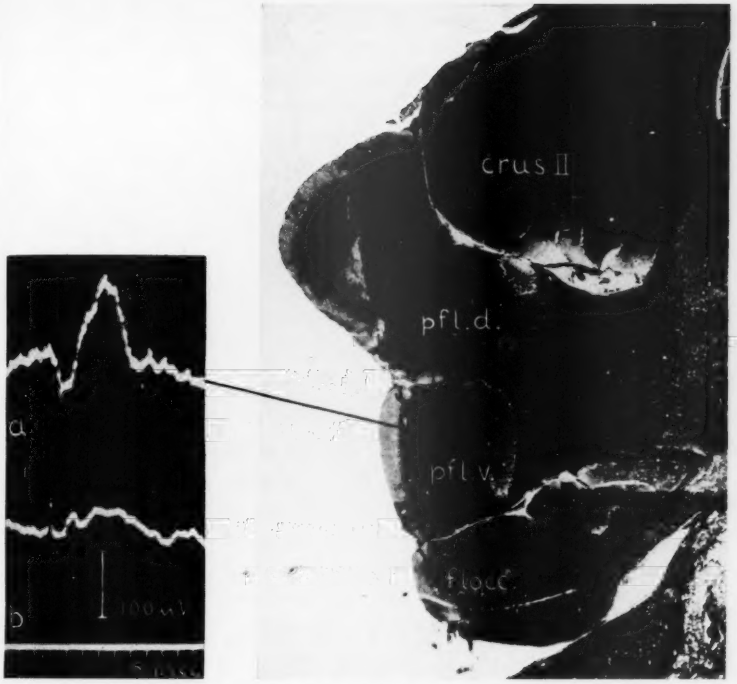


Fig. 15. Section showing penetrating electrode track through the dorsal into the ventral paraflocculus. Records from the ventral paraflocculus (pfl.v.) after stimulation of lateral part of contralateral anterior sigmoid gyrus, (a) before, (b) after electrolysis at the recording electrode tip.

the dorsal paraflocculus. The position of the electrode tip was checked histologically (fig. 15). Only the posterior half of the ventral paraflocculus was explored in the present experiments.

The potentials recorded in the ventral paraflocculus following cortical stimulation were always quite small (fig. 15) in spite of good responsiveness of the rest of the cerebellar hemisphere. The responses were elicited from a rather small cortical area in the lateral part of the contralateral anterior sigmoid gyrus (fig. 16).

The latency of the potentials was between 3 and 5 msec. It was considered possible that the small responses in the ventral paraflocculus might represent physical spread of distant electrical activity. The experiment shown in fig. 15 makes this assumption less likely. The ventral paraflocular response was almost completely

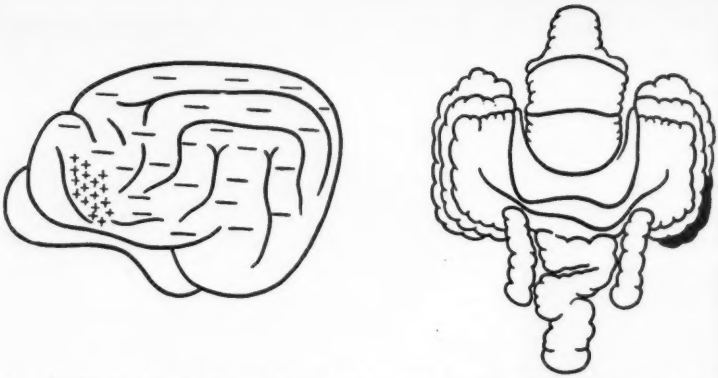


Fig. 16. Cerebral cortical areas from which responses were elicited in the posterior part of the ventral paraflocculus. Symbol explanation in fig. 13.

abolished following electrolysis at the recording electrode tip. Prominent surface responses in the dorsal paraflocculus following stimulation of the anterior part of the lateral gyrus disappeared when the recording electrode reached the ventral paraflocculus. This observation also favours the opinion that the recorded potentials represent local activity.

Stimulation of the medial surface of the hemisphere and of the lateral surface outside the area mentioned above did not evoke activity in the posterior part of the contralateral ventral paraflocculus. Stimulation of the ipsilateral hemisphere has not been carried out while recording from the ventral paraflocculus.

The small size of the ventral paraflocculus response on cortical stimulation suggests that this part of the cerebellum receives its main afferents from other sources than the cerebral cortex. The possibility of afferents from spinal levels was, therefore, tested by stimulating the contralateral and ipsilateral radial and sciatic nerves. Prominent responses were evoked at the insertion point in the dorsal (unpublished observations) but none in the ventral paraflocculus, nor did stimulation of the ipsilateral vagal nerve yield responses in the ventral paraflocculus.

(c) Crus II

Large action potentials were readily obtained in the crus II of the ansiform lobule on stimulating rather extensive, but distinct areas of the cerebral cortex. The potentials were most often of the

combined short- and long-latency type, but the other categories of potentials described above were also frequently encountered (fig. 1, records A2, C2, D2). At a certain critical level of anaesthesia there was a difference in the distribution of the cerebral cortical areas yielding potentials in the postero-medial and the antero-lateral parts of the crus II (fig. 17 and 18). The boundary between these two cerebellar areas was not distinct and differed a little from experiment to experiment.

(i) *Postero-medial part of the crus II.* — The greatest potentials were recorded in this part of the cerebellum on stimulating the lateral part of the contralateral anterior sigmoid gyrus. The excitable area extended from the presylvian sulcus anteriorly and comprised the lateral part of the anterior sigmoid, the anterior parts of the orbital and anterior ectosylvian gyri and the most lateral portion of the posterior sigmoid gyrus (fig. 17). These potentials as a rule were of the long-latency variety (10–12 msec.) (fig. 1, record A2), but combined short- and long-latency potentials were also frequently obtained, especially from the anterior ectosylvian gyrus (fig. 1, record C2). From the anterior suprasylvian gyrus pure short-latency responses (3–5 msec.) were generally elicited.

Stimulation of the posterior sigmoid gyrus and the lateral gyrus occasionally evoked small action potentials in the crus II, but in most experiments these areas proved unresponsive. Stimulation of the medial surface of the hemisphere failed to elicit action potentials in the postero-medial part of the crus II.

In conformity with the findings in the dorsal paraflocculus, action potentials in the crus II could also be obtained on stimulating the ipsilateral hemisphere. The excitable areas were located symmetrically in relation to the most excitable areas in the contralateral hemisphere. The ipsilateral responses generally were of smaller amplitude and sometimes of a slightly longer latency than the contralateral ones.

(ii) *Antero-lateral part of the crus II.* — The cortical areas yielding responses in the antero-lateral and postero-medial parts of the crus II were not quite coextensive. Long-latency potentials, or occasionally combined short- and long-latency potentials, were readily elicited in the lateral part of crus II from the medial part of the contralateral anterior sigmoid gyrus. Furthermore, such potentials

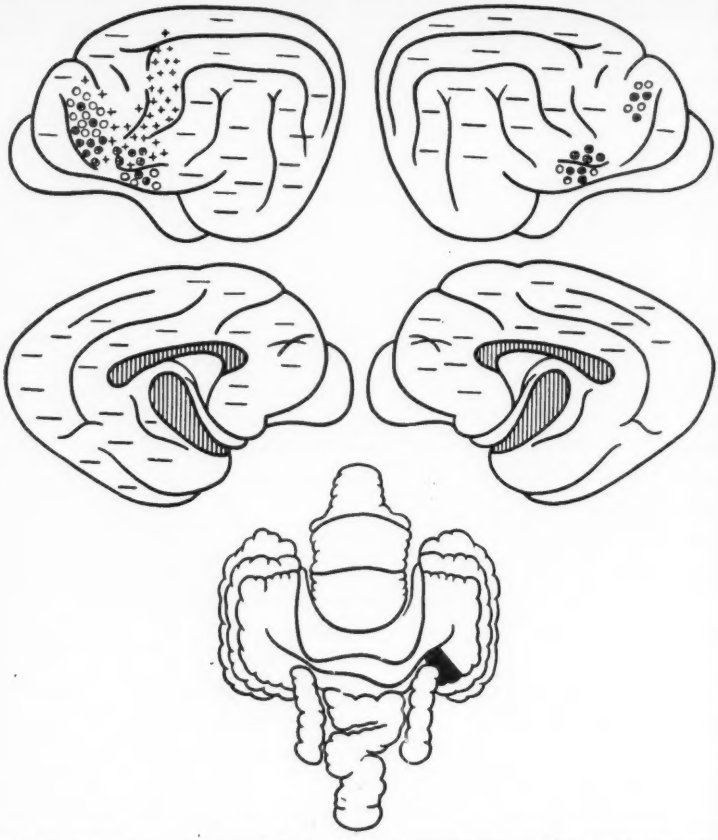


Fig. 17. Cerebral cortical areas from which responses were elicited in the posteromedial part of crus II. Symbols as in fig. 13.

were evoked from a very narrow zone close to the presylvian sulcus (fig. 18). This area continued posteriorly into the orbital gyrus. Long-latency potentials were also elicited from an area in the proreate and anterior limbic gyri of the medial surface of the hemisphere (fig. 18). Short-latency potentials were elicited in this cerebellar area from the posterior part of the anterior ectosylvian and from a small part of the anterior sylvian gyrus.

Stimulation of the ipsilateral hemisphere also evoked potentials in the lateral part of crus II. The excitable areas were less extensive in the ipsilateral hemisphere and corresponded to those in the con-

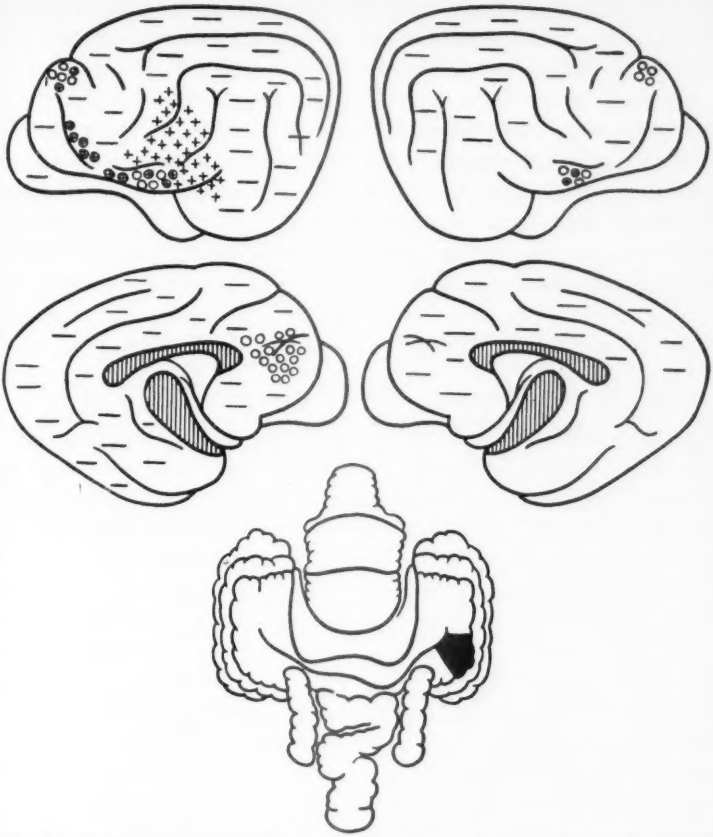


Fig. 18. Cerebral cortical areas from which responses were elicited in the antero-lateral part of crus II. Symbols as in fig. 13.

tralateral yielding the most prominent and constant responses in this cerebellar area (fig. 18).

The crus II proved unresponsive to stimulation of other areas of the cerebral cortex than those mentioned above.

(d) Crus I

Potentials in response to stimulation of the cerebral cortex were less readily obtained from the crus I, and they were of smaller amplitude than those recorded from the crus II. This may possibly

be due to the greater technical difficulties involved in the exposure of this part of the cerebellum. In most of the present experiments only the posterior part of the lobule was exposed. The potentials recorded from the crus I were often surface negative. Long-latency potentials were elicited from the lateral part of the contralateral anterior sigmoid gyrus, especially in its rostral portion close to the presylvian sulcus (fig. 1, record A1). The same area may evoke combined short- and long-latency potentials. This was also the most common response in the crus I on stimulation of the anterior part of the orbital gyrus. Stimulation of the anterior ectosylvian

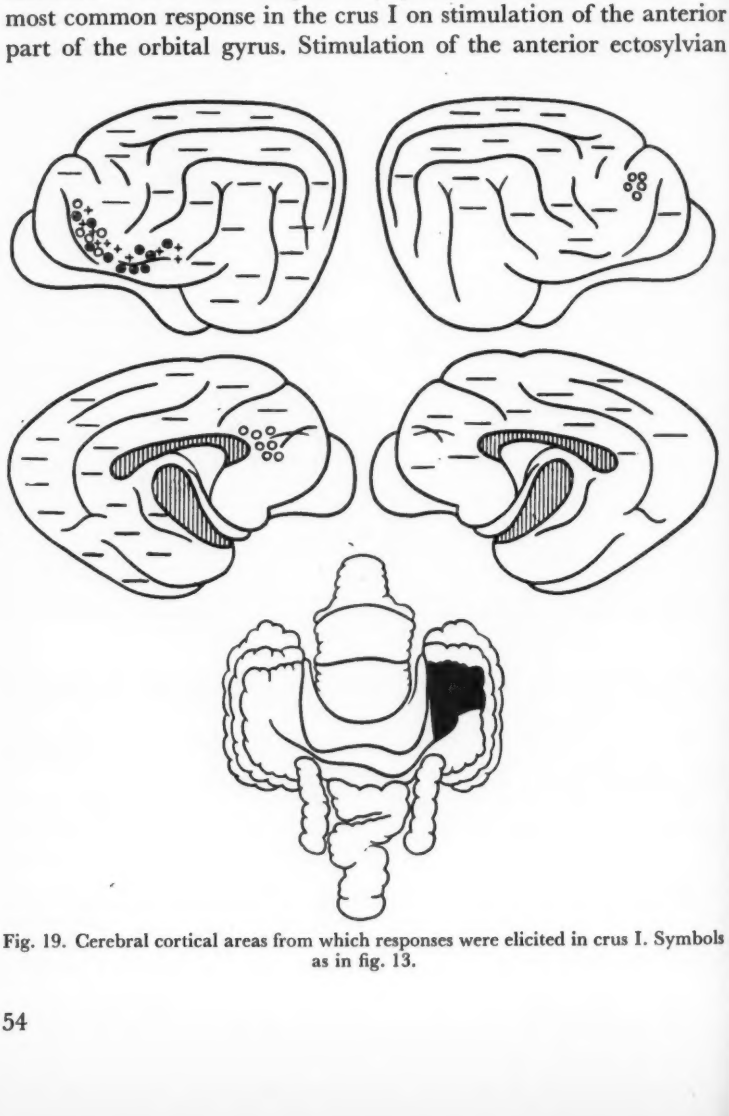


Fig. 19. Cerebral cortical areas from which responses were elicited in crus I. Symbols as in fig. 13.

gyrus, however, often evoked pure short-latency potentials in the crus I (fig. 19). This response was also occasionally encountered following stimulation of the effective zone in the anterior sigmoid gyrus. From the medial surface of the hemisphere long-latency potentials (15 msec.) were obtained in the crus I from an area confined to a rather limited part of the anterior limbic and proreate gyri close to the genus corporis callosi (fig. 19). From the ipsilateral hemisphere long-latency potentials were elicited in the crus I from a small area of the anterior sigmoid gyrus (fig. 19).

Stimulation of other areas of the cerebral cortex did not evoke responses in the crus I of the ansiform lobule.

(e) Paramedian lobule

Following stimulation of the cerebral cortex, action potentials were more readily obtained in the paramedian lobule than in any other part of the cerebellar hemisphere explored in the present experiments. Generally the potentials were of rather great amplitude. As described by Dow (1942) and Snider and Eldred (1951) there is a difference in the distribution of cortical areas evoking action potentials in the anterior and posterior parts of the lobule in anaesthetized animals.

(i) *Anterior part of the paramedian lobule.* — Potentials were recorded from this area on stimulation of a rather extensive area in the contralateral cerebral hemisphere (fig. 20). Long-latency potentials predominated following excitation of the more lateral parts of the anterior and posterior sigmoid gyri (fig. 1, record A4), sometimes also on stimulation of the anterior part of the orbital gyrus. Combined short- and long-latency potentials were frequently obtained from the most lateral portion of the sigmoid gyri and the adjacent portion of the anterior ectosylvian gyrus. Short-latency potentials were elicited by stimulation of the posterior part of the posterior sigmoid gyrus just in front of the ansate sulcus, the neighbouring part of the lateral and suprasylvian gyri and from the anterior part of the anterior ectosylvian gyrus (fig. 1, record C4). In more lightly anaesthetized animals the entire paramedian lobule could be excited from the entire anterior ectosylvian gyrus (cf. fig. 22). The responses from the posterior part of this gyrus had, however, a higher threshold than those from the anterior part. Removal of the low-

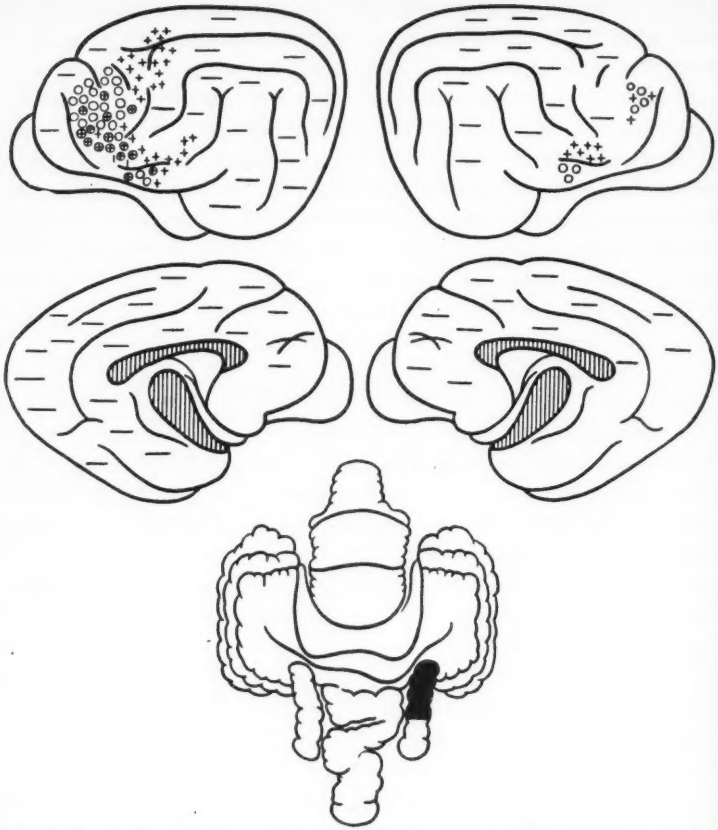


Fig. 20. Cerebral cortical areas from which responses were elicited in the anterior part of paramedian lobule. Symbols as in fig. 13.

threshold anterior region by suction proved that the high-threshold responses from the posterior part do not represent spread of the stimulating current, as this procedure was without any influence on the high-threshold responses from the posterior zone.

Responses to stimulation of the ipsilateral hemisphere were more readily obtained from the paramedian lobule than from any other portion of the cerebellar hemisphere explored in these experiments. The most excitable areas corresponded to those in the contralateral hemisphere giving the largest and most constant responses in the anterior paramedian lobule (fig. 20). The ipsilateral responses were

as a rule of smaller amplitude than the contralateral ones, and their latencies were frequently slightly longer (fig. 25). Sometimes, however, the latencies were the same in both paramedian lobules on stimulating the same point in the cerebral cortex.

(ii) *Posterior part of the paramedian lobule.* — Long-latency potentials were readily recorded from this portion on stimulation of the medial part of the anterior and posterior sigmoid gyri on the contralateral side (fig. 21). The excitable area extended onto the medial surface of the hemisphere posterior to the cruciate sulcus. Long-

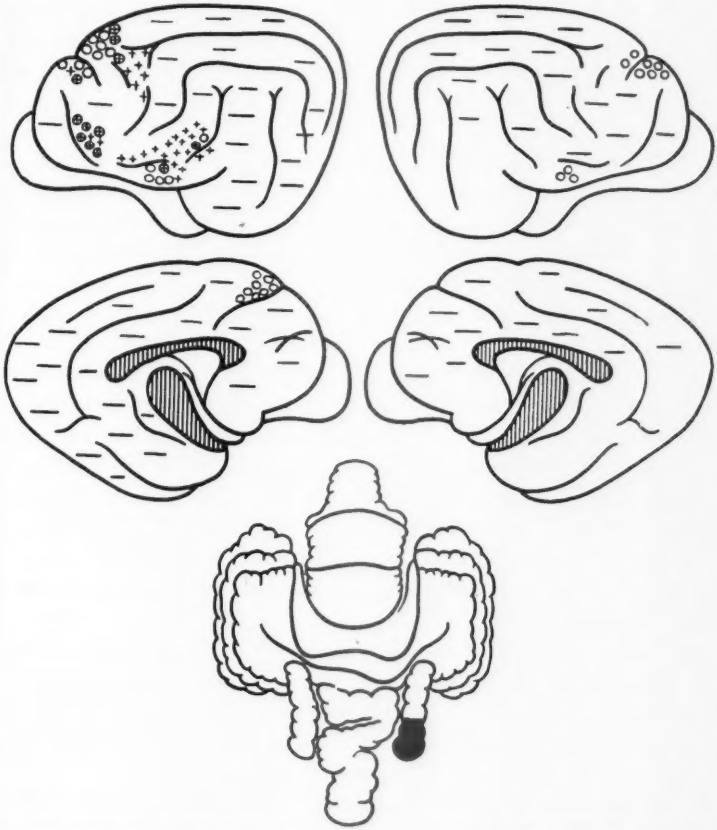


Fig. 21. Cerebral cortical areas from which responses were elicited in the posterior part of paramedian lobule. Symbols as in fig. 13.

latency potentials were also seen following stimulation of the posterior part of the orbital gyrus. From the anterior part of the orbital gyrus, potentials were evoked only in the anterior part of the paramedian lobule. Combined short- and long-latency potentials were recorded from the posterior part of the paramedian lobule on stimulation of a rather narrow zone just posterior to the presylvian sulcus (fig. 21) and also from the posterior and lateral border of the sigmoid area yielding long-latency responses.

Short-latency responses were obtained in this cerebellar area by stimulating the area just anterior to the ansate sulcus (fig. 21). Such potentials were also elicited from the posterior part of the anterior ectosylvian gyrus. Occasionally also combined short- and long-latency potentials were induced from this region. Except for the small zone just posterior to the cruciate sulcus, stimulation of the medial surface of the hemisphere did not evoke any responses in the paramedian lobule.

Following stimulation of the ipsilateral cerebral cortex only long-latency potentials were elicited in the posterior paramedian lobule. The excitable areas were confined to the medial part of the anterior and posterior sigmoid gyri and to the orbital gyrus. The ipsilateral anterior ectosylvian gyrus gave no responses.

Combs (1954) found, in unanaesthetized cats, a diffuse distribution of spinal impulses in the anterior lobe. In view of Comb's observations it was considered of interest to examine the distribution of cortical impulses in the cerebellar hemisphere of animals not depressed by Nembutal. Four experiments were performed with chloralose anaesthesia only and immobilization by decamethonium. As the paramedian lobule was the part of the cerebellar hemisphere which displayed the sharpest localization following cortical stimulation (see above) special attention was paid to this lobule in these experiments.

The effective cortical area yielding responses in the contralateral paramedian lobule in the chloralose anaesthetized animals appeared practically to coincide with that outlined above (figs. 20, 21). In these experiments, however, every point within the effective cor-

Fig. 22. Distribution of responses in paramedian lobule in chloralose-anaesthetized cat. (a) Before, (b) after administration of Nembutal (10 mg/kg). Stimulation of points A and B in contralateral anterior ectosylvian gyrus. — (A) Responses in different folia to stimulation of point A. — (B) Responses to stimulation of B.

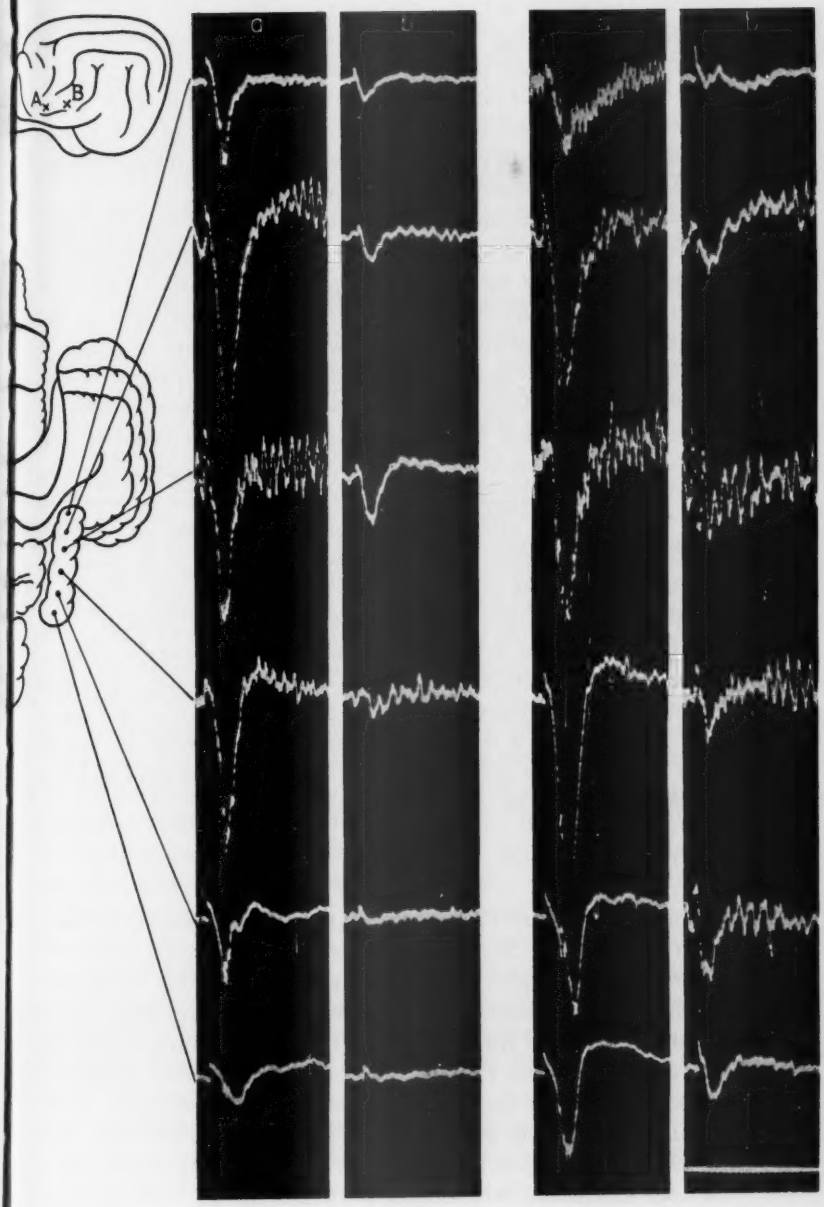


Fig. 22.

tical zone seemed to activate the entire or the major part of the paramedian lobule (fig. 22). In the chloralose anaesthetized animals the potentials were generally of the combined short- and long-latency or pure short-latency type. Occasionally the pure long-latency potentials were observed, especially following stimulation of the anterior sigmoid gyrus, but combined short- and long-latency potentials predominated from this area as well.

Following administration of Nembutal to such a chloralose preparation displaying diffuse responses all over the paramedian lobule, the responses became more localized and were greatly reduced in amplitude. Fig. 22 illustrates the distribution of responses in the contralateral paramedian lobule following stimulation of points A and B in the anterior ectosylvian gyrus. Stimulation point A was probably within the face or foreleg subdivision of somatica area II and point B within the hindleg area as outlined by Woolsey and Fairman (1946). Before intravenous Nembutal administration, point A as well as point B activated all the surface folia of the paramedian lobule. Ten minutes after the injection of Nembutal (10 mg/kg) the responses to stimulation of point A were localized in the anterior part of the paramedian lobule, whereas the responses were obtained in the posterior part of the lobule on stimulation of point B.

The possibility that the diffuse paramedian responses in chloralose anaesthetized animals were due to cerebellar cortical spread of the activity was ruled out by ablation of various parts of the paramedian lobule. Thus a lesion of the anterior portion of the lobule did not eliminate the responses in the posterior part evoked from the anterior part of the anterior ectosylvian gyrus.

(2) Discussion

As described by Dow (1942), stimulation of the sigmoid, coronal, anterior part of the lateral, the anterior suprasylvian and the anterior ectosylvian gyri may evoke potentials in the cerebellar hemispheres. In addition the present experiments have demonstrated a projection from the orbital gyrus and, confirming Hampson (1949) and Snider and Eldred (1951), from the medial surface of the hemisphere to the cerebellum. Stimulation of other parts of the cerebral cortex did not evoke responses in those parts of the cerebellar hemisphere which were explored in the present experiments.

To some extent contrary to Dow's (1942) conclusions it has been

possible in cat under a critical depth of anaesthesia to demonstrate certain topographical relationships between cerebral and cerebellar cortices, and in the following an attempt will be made to correlate the findings to the known functional zones in the cerebral cortex.

The *anterior sigmoid gyrus*, which corresponds to the classical motor area, has been shown to activate at least parts of all the cerebellar lobuli under consideration. The area giving the most widely distributed potentials is situated in a narrow zone just posterior to the presylvian sulcus laterally, apparently corresponding to the face area (Garol 1942a).

In confirmation of the findings of Snider and Eldred (1951) stimulation of the medial part of the motor cortex (leg area) evoked long-latency potentials from the posterior part of the paramedian lobule (fig. 21), whereas the arm area activates the anterior part of the same lobule (fig. 20). A corresponding somato-topic relation is observed in the crus II, the antero-lateral part of which seems to be related to the leg area (fig. 18) and the postero-medial part to the arm area (fig. 17). This localization within the crus II is not, however, as easily revealed as that of the paramedian lobule.

As regards the *posterior sigmoid gyrus*, the sensory somatic area I of Woolsey and Fairman (1946), it is evident that stimulation of this area activates the paramedian lobule in a similar manner as does the motor area: the medial parts of the gyrus project to the posterior parts of the paramedian lobule (fig. 21), and the lateral parts of the posterior sigmoid gyrus project onto the anterior parts of the same lobule (fig. 20). But in contrast to the anterior sigmoid, the posterior sigmoid gyrus does not seem to activate the ansiform lobule to any significant extent (figs. 17–19). Only very small potentials may occasionally be recorded from the ansiform lobule on stimulating the sensory somatic area I.

The most posterior part of the posterior sigmoid gyrus, just anterior to the ansate sulcus, seems to activate the cerebellum in a way which differs from the rest of the sigmoid gyrus. This area, apparently corresponding to the "somatic area III" (Marshall, Woolsey and Bard 1941; Marshall 1949) evokes short-latency potentials all over the paramedian lobule (figs. 20–21) while the ansiform lobule is unresponsive (figs. 17–19). There is no sign of a somatotopic localization in the paramedian lobule on stimulation of different points of this area. In the "somatic area III" there is a convergence of spinal impulses from all four limbs (Amassian 1954),

and it is interesting to note that its projection to the paramedian lobule reveals no sign of localization.

Stimulation of the *anterior part of the lateral gyrus* evokes a short-latency response in the posterior folia of the dorsal paraflocculus (fig. 13) and sometimes in the anterior part of the paramedian lobule (fig. 20), whereas the other parts of the cerebellar hemisphere remain unresponsive. This part of the cerebral cortex apparently corresponds to the area where Purpura (1955) found a maximal area for the "secondary response" following stimulation of spinal nerves. This area also appears to be related to the "suppressor area" 2S (Garol 1942a, b) and to the zone from which Eliasson (1954) obtained increase of gastric motility.

From the *anterior ectosylvian gyrus*, apparently corresponding to the sensory somatic area II of Woolsey and Fairman (1946), it is possible to activate extensive parts of the paramedian and ansiform lobules (figs. 17–21). In agreement with Hampson (1949) the potentials elicited from the somatic area II of the cerebral cortex were generally of the short-latency type, whereas the somatic area I on stimulation evoked predominantly long-latency potentials in the cerebellum. Also, the localization of the responses was much less evident on stimulating arm and leg areas of the somatic area II as compared to the somatic area I. Snider and Eldred (1951) were unable to demonstrate a somato-topical localization in the paramedian lobule on stimulating the sensory somatic area II. The present investigation, however, lends support to Hampson's view (1949). In a critical depth of anaesthesia, with careful attention to threshold stimuli, this author was able to demonstrate that the arm area of the somatic area II activates the more anterior folia of the paramedian lobule and the leg area the more posterior folia (fig. 22). In the present investigation it was also possible, under similar conditions, to demonstrate that the arm subdivision of the somatic area II predominantly activated the medial part of the crus II while the leg area activated the lateral part of the same lobule.

From the *orbital gyrus* it proved possible to evoke rather widespread responses in the cerebellar hemisphere both of the short- and long-latency type. The following observations indicate that the responses are not due to spread of the stimulating current to the adjacent somatic area II. (i) The threshold is about the same for the two areas. (ii) Stimulation of the orbital gyrus evokes responses in the dorsal paraflocculus. These responses are not elicited from

the anterior ectosylvian gyrus. (iii) From the orbital gyrus long-latency responses are frequently recorded, whereas these are rarely seen following somatic II stimulation. (iv) The response elicited from the orbital gyrus may have a long unresponsive time in contrast to that induced from the anterior ectosylvian gyrus.

As previously shown by Hampson (1949) and Snider and Eldred (1951) it is possible to activate the ansiform lobule from the *medial surface* of the hemisphere. The present investigation has shown that the same cortical area, namely part of the anterior limbic and proreate gyri, may also activate the dorsal paraflocculus. In contrast to Snider and Eldred (1951) the responses were recorded more readily from the lateral part of the ansiform lobule than from the medial part.

As described above, the dorsal paraflocculus may be activated from several cortical regions: an area adjacent to the presylvian sulcus, the anterior part of the lateral gyrus, the orbital and the anterior limbic gyri. From all these parts of the cerebral cortex it has been possible on stimulation to produce alterations in respiratory movements and induce a variety of autonomic effects (for references, see Kaada 1951; Eliasson 1954). Therefore, the possibility that the paraflocculus has something to do with the regulation of autonomic activities deserves consideration in future physiological experiments on this portion of the cerebellum. On the other hand, the maps of the cortical regions from which "the recruiting response" may be recorded on thalamic stimulation (Starzl and Magoun 1951) reveal a striking resemblance to those of the cortical zones from which responses may be evoked in the dorsal paraflocculus (figs. 13 and 14). Stimulation of the small area in the posterior suprasylvian gyrus (Starzl and Magoun 1951) did not, however, yield any parafloccular responses.

The possibility of longitudinal subdivisions of the paramedian lobule, as described by Szabo and Albe-Fessard (1954) for the spinal impulses, was frequently looked for in the present study. On stimulation of the cerebral cortex, however, it has not been possible to define the α, β and γ subdivisions described by Szabo and Albe-Fessard. The impression has been gained that most of the short-latency responses evoked from the cerebral cortex were found medially in the paramedian lobule, but not with a constancy sufficient to permit a subdivision of the lobule on this basis.

The experiments performed under chloralose anaesthesia with

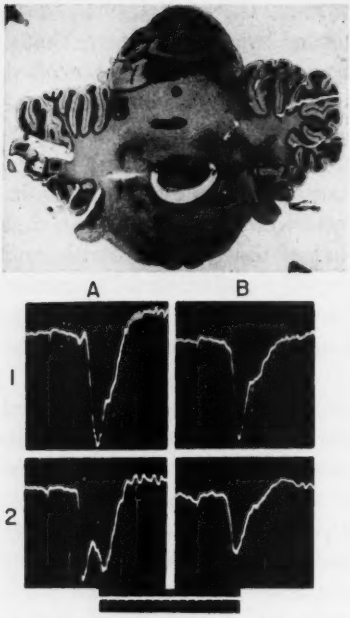


Fig. 23. Long-latency potentials in the paramedian lobule (1) and the crus II (2) evoked by stimulation of the contralateral anterior sigmoid gyrus. — (A) Before, (B) after lesion of the restiform body, indicated by arrow in the section above. A few of the most lateral fibres of the restiform body were not included in the lesion.

additional administration of Nembutal demonstrate for the cortico-cerebellar pathways what Combs (1954) has shown for the spino-cerebellar impulses, viz. the existence of diffuse as well as more localized responses. However, in the author's opinion, that does not necessarily imply that the diffuse and localized responses are mediated via different cortico-cerebellar pathways, as suggested by Combs (1956) for the spino-cerebellar impulses. It seems more likely that the explanation is to be found in a quantitative difference in the connections between the different regions. When the general responsiveness of the central nervous system is reduced by Nembutal, impulses are only transmitted between the regions most heavily interconnected.

(C) Cortico-cerebellar pathways

As regards the pathways mediating the cortico-cerebellar impulses, several possibilities exist. Dow (1942) assumed that both the short- and long-latency responses were mediated via the pontine nuclei. Snider and Stowell (1951, 1952) maintained a similar view, although without any experimental verification. The recent study of Walberg (1956) suggests the possibility that the cortical impulses to the paramedian lobule and the crus II of the ansiform lobule may also be mediated via the inferior olive, although the cortico-olivary fibres are comparatively few. The possibility of a multisynaptic transmission must also be kept in mind, although it appears less likely.

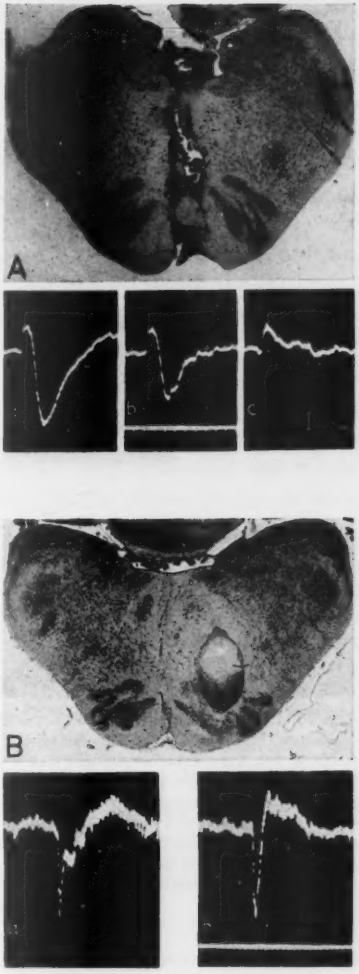


Fig. 24. Lesions of the inferior olive with no influence on the cortico-cerebellar responses. — (A) Complete mid-sagittal section between the inferior olives. Short-latency response in paramedian lobule to stimulation of contralateral anterior ectosylvian gyrus. (a) Before, (b) after lesion showed in A. (c) After lesion of ipsilateral pontine brachium. — (B) Olivary lesion including the ventral lamella projecting to paramedian lobule. Long-latency responses in paramedian lobule to stimulation of contralateral anterior sigmoid gyrus. (a) Before, (b) after lesion in B.

In order to determine the rôle of the pontine nuclei, the inferior olivary and possible brain stem nuclei in the transmission of cortico-cerebellar impulses, various acute lesions were made in the cerebellar peduncles and in the brain stem.

In several experiments it has been shown that when all the cerebellar peduncles are cut on one side, all cortico-cerebellar action potentials are completely abolished in the cerebellar hemisphere on the same side. If, however, as shown in fig. 23, the fibres running in the restiform body are cut, only very small and insignificant changes are observed in the long-latency action potentials recorded from (1) the paramedian lobule and (2) the crus II (A, before; B, after the lesion). According to generally accepted anatomical views this rules out the olive and the lateral reticular nucleus as a pathway for these impulses. Mid-sagittal severance of the decussating olivo-cerebellar fibres and other olivary lesions also indicated that the short-latency as well as the long-latency cortico-cerebellar potentials most likely are independent of the olive (fig. 24). On the other

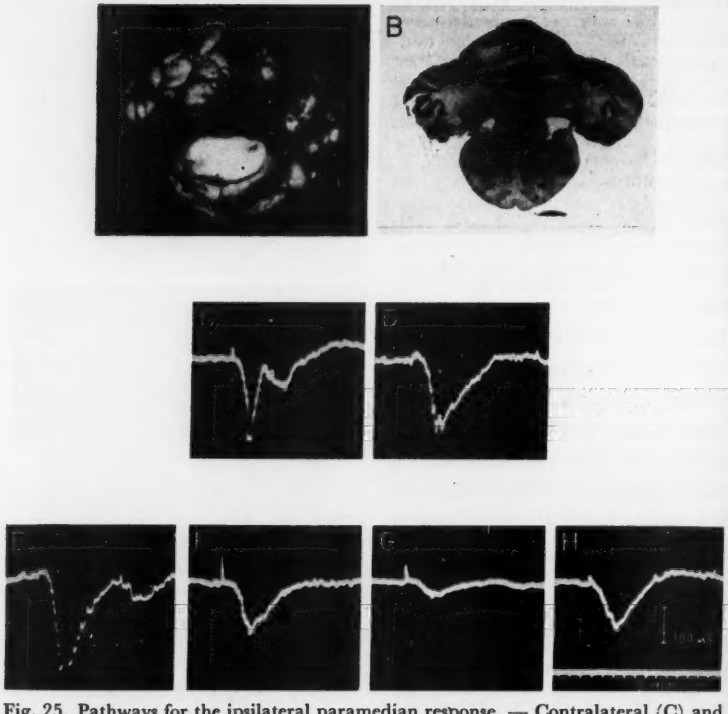


Fig. 25. Pathways for the ipsilateral paramedian response. — Contralateral (C) and ipsilateral (D) responses in paramedian lobule to stimulation of the same cortical point in the anterior ectosylvian gyrus. — (E) Ipsilateral response still present after a lesion of the contralateral paramedian lobule shown in (A). — (F) Same response reduced, but probably not to a significant degree following midsagittal section of cerebellum indicated by arrows in (B). — (G) Same response almost eliminated after a lesion of the ipsilateral cerebellar peduncles. — (H) Response in the contralateral crus II showing that the cerebellum was still responsive. The small trace of response left in (G) was probably due to a few fibres of the pontine brachium not included in the lesion.

hand, after lesions in the pontine brachium, both short- and long-latency cortico-cerebellar responses were abolished. It may be concluded, therefore, that the short- and long-latency potentials in the cerebellar hemisphere, elicited from the contralateral cerebral cortex, probably are mediated via the pontine nuclei.

Another problem is why ipsilateral responses are more readily obtained in the paramedian than in the ansiform lobule on cortical stimulation and how the ipsilateral impulses reach the cerebellum. The available anatomical data contribute little to explain this point.

It has been suggested (Brodal 1949) that responses may be relayed between the two paramedian lobules. Jansen (1933) has described such a commissure in rabbits. The fact that the ipsilateral response generally has a longer latency than the contralateral one is in favour of this view. Sometimes, however, the two responses have the same latency. An experiment was carried out as shown in fig. 25. A potential was recorded in both paramedian lobules on stimulating the same cortical point (fig. 25, C, contralateral; D, ipsilateral). A complete lesion of the paramedian lobule contralateral to the point stimulated (A) did not influence the ipsilateral response (E). The possibility that the impulses cross in the cerebellum was ruled out by a mid-sagittal section of the cerebellum (B). This reduced the amplitude of the ipsilateral response (F) but to a degree that is probably not significant. A lesion of the ipsilateral cerebellar peduncles almost completely abolished the response (G). The little response left in record G is probably due to the incompleteness of the lesion. Some of the fibres of the pontine brachium had been left intact. Records from the contralateral ansiform lobule showed that the cerebellum was still responsive (H).

Two possible pathways now remain for the ipsilateral paramedian response. (i) There is a double crossing, the first between the cerebral cortex and the pons, the next between the pons and the paramedian lobule. (ii) The impulses do not cross at all. Anatomical evidence makes both possibilities seem equally likely (Brodal and Jansen 1946; Nyby and Jansen 1953). Attempts to elucidate this problem by placing midagittal lesions in the pons have been unsuccessful. They always resulted in complete unresponsiveness of the preparation.

Chapter IV

Cerebellar responses to stimulation of brain stem nuclei

(1) Pons

Stimulation of the pontine nuclei evokes characteristic and widespread responses in the cerebellar hemispheres (fig. 26). The most prominent responses were in general obtained from the contralateral paramedian lobule and the medial part of the crus II, irrespective of the pontine point stimulated. No attempts were made to record from the ventral paraflocculus after stimulation of the pons and the other brain stem nuclei investigated. Smaller responses were obtained in the lateral part of crus II, the crus I and the dorsal paraflocculus. Ipsilateral cerebellar responses were most readily found in the paramedian lobule following stimulation of the ventral parts of the pontine nuclei. Smaller ipsilateral responses were encountered in the crus I and II.

The typical responses consisted of a surface-positive wave of very short latency (1–2 msec.), the duration of which varied between 15 and 30 msec. The amplitude of this wave was comparatively small, seldom exceeding 300 μV. recorded with surface electrodes. Sometimes a sharp spike preceded the wave component (fig. 28A). The amplitude of this spike could vary considerably as compared to the slow wave. In many instances the initial spike was hardly distinguishable from the shock-artefact (fig. 27). The spike and wave were found to have approximately the same threshold. Occasionally a long-latency (15–20 msec.) quite sharp component was seen in the later part of the broad wave (fig. 28B). This deflection is generally of small amplitude and was quite unstable. The threshold of this long-latency deflection was higher than that of the broad wave.

Surface-negative potentials were also found following stimulation of the pontine nuclei. These responses consisted of the same components and had the same latencies as the surface-positive poten-

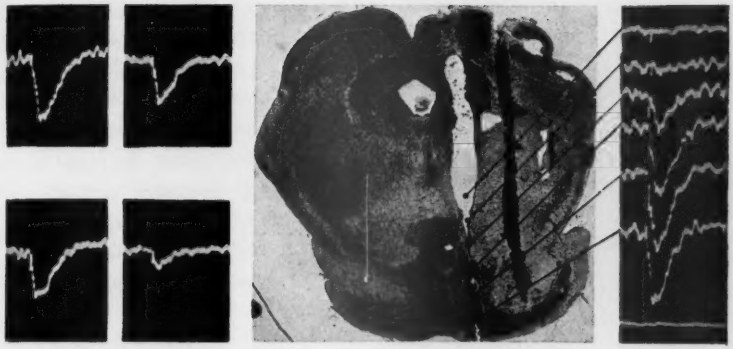
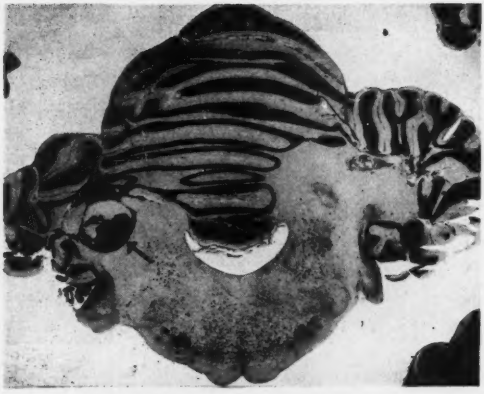


Fig. 26. Cerebellar responses to pontine stimulation. — (A) Contralateral (a) and ipsilateral (b) responses in paramedian lobule (lob.p.m.) and crus II. — (B) Stimulated points (1 mm apart) and corresponding records obtained in contralateral paramedian lobule. Another electrode track is seen laterally in the brain stem section. From the most ventral parts of this smaller responses were obtained in the cerebellar hemisphere.

tials. They have been recorded from all the cerebellar lobules examined, but were most-often encountered in the crus I and the lateral part of crus II of the ansiform lobule.

Some of the characteristics of responses in the cerebellar hemisphere to pontine stimulation have been examined following local application of strychnine and novocaine on the cerebellar cortex. The effect of asphyxiation of the animal and of double shock stimulation has also been tested.

The effect of local cerebellar *strychninization* on the paramedian response to pontine stimulation is shown in fig. 27 A. The potential consisted of an initial sharp spike barely recognizable and a broad wave. After 8 minutes of strychninization the initial spike remained practically unchanged whereas the duration of the broad wave was decreased. After 10 minutes the wave gradually reappeared with a considerable increase in duration, and in the last record, after 30 minutes there was a significant increase of the slow wave, both in amplitude and duration. The initial spike, however, remained practically unchanged during the experiment. No late surface-negative wave appeared in the ponto-cerebellar evoked potentials on strychninization. The cerebellar cortex was then washed with heated Ringer solution and *novocaine* was applied to the cerebellar lead point. Not until 15 minutes after the application of novocaine did a depression of the slow wave become evident, and after 20 minutes



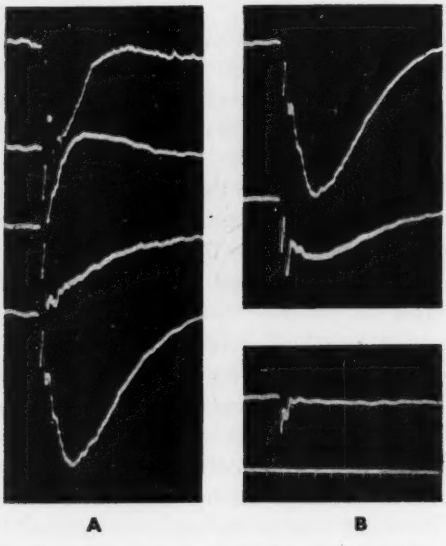


Fig. 27. Effect of local application of strychnine and novocaine on paramedian response to contralateral pontine stimulation. — (A) Top record, control. Subsequent records, 8, 10 and 30 min. after strychnine application. — (B) Same response as in A. Cortex washed with Ringer solution. Strychnine effect still present. Top record, before; second record, 20 min. after application of novocaine. Last record, no response left after lesion of ipsilateral pontine brachium seen in section above, indicated by arrows.

this depression was well-marked (fig. 27 B). The initial spike, however, was apparently little influenced by the depressing action of novocaine. A lesion of the brachium pontis (fig. 27) eliminated both the initial spike and the rest of the long-lasting wave as the last record of fig. 27 B illustrates.

The effect of *asphyxia* upon the ponto-cerebellar potentials is shown in fig. 28. The potential in column A consisted of an initial sharp spike and a late wave. After 2 and 3 minutes of asphyxiation a small depression of the wave component was discernible. The following record, however, taken after 4 minutes, exhibits a definite increase in the amplitude of the wave. As suggested for the cortico-cerebellar potentials, this may be due to the excit-

atory action of the increased CO_2. After 5 minutes of asphyxiation there was a great reduction of both the spike and the wave component of the response, and after 6 minutes they had both disappeared. The last record shows the recovery of the potentials after 7 minutes of artificial respiration.

Fig. 28B demonstrates the changes taking place during asphyxiation in a ponto-cerebellar evoked potential consisting of both short- and long-latency deflections. Already after 2 minutes of asphyxiation a definite decrease in the amplitude of the long-latency component was noted. After 3 minutes of asphyxiation this deflection was completely blocked. At the same time the short-latency wave was also considerably depressed and apparently divided into two different fractions, the later of which was more depressed than the former. In the following record (4 minutes) this second fraction of the short-latency component was completely abolished, and there was a further decrease in the amplitude of first part of this wave. After 6 minutes of asphyxiation there was little left also of the initial part of the short-latency wave, and the next record shows the recovery of the potential following 5 minutes of artificial respiration. The last record shows the complete disappearance of the potential after a lesion in the ipsilateral cerebellar peduncles.

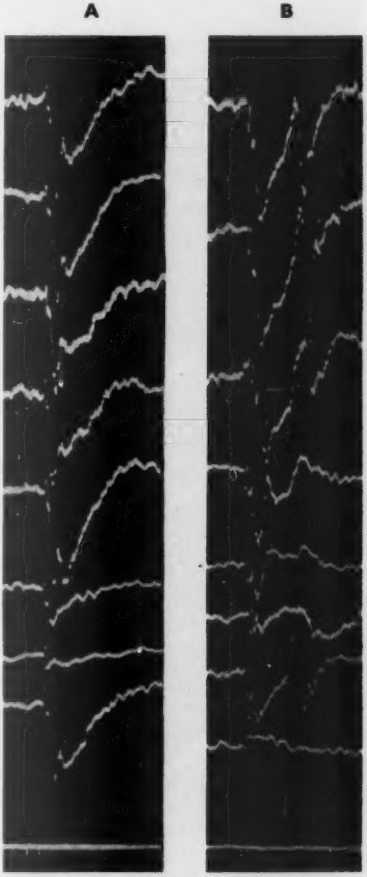
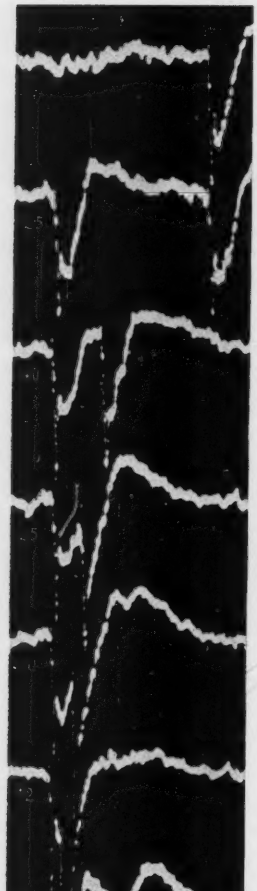


Fig. 28. Effect of asphyxia upon responses in paramedian lobule to contralateral pontine stimulation. Top records, control before asphyxiation. Duration of asphyxia in minutes below each record. — (A) Last record, recovery after 7 min. artificial respiration. — (B) Another experiment. Last record, complete disappearance of response after lesion of the ipsilateral cerebellar peduncles.



In the earliest part of the short-latency wave it is possible to recognize a very sharp positive component which is barely distinguishable from the shock artefact. This component was progressively reduced together with the short-latency wave after 3 and 4 minutes of asphyxia. From 4 to 6 minutes of asphyxia, however, there was little reduction of this component whereas the wave exhibited a considerable further depression. The last record taken after a lesion in the cerebellar peduncles shows that the initial spike-like component was not a part of the shock artefact as it disappeared after this lesion.

The cerebellar responses to *double shock* pontine stimulation are illustrated in fig. 29. Shock intervals are given in msec. below each record. The unconditioned response seen in the top record consisted of an initial spike and a late wave. As the shock interval was decreased there was a decrease in the duration of the second response, best seen in records 20 and 12 msec. Little change is observed in the initial spike. The second wave appearing in the last record (2 msec.) is sometimes seen following pontine stimulation with double shocks at short intervals.

The *interaction* between cerebellar potentials evoked from the pontine nuclei and the cerebral cortex has also been investigated (fig. 30). In column A the conditioning response elicited from the pontine nuclei consisted of a simple positive wave. The test response was of the long-latency type elicited by stimulation of the posterior

Fig. 29. Response in paramedian lobule to double shock contralateral pontine stimulation. Top record, test response only. Interval between shocks indicated in msec. below each record.

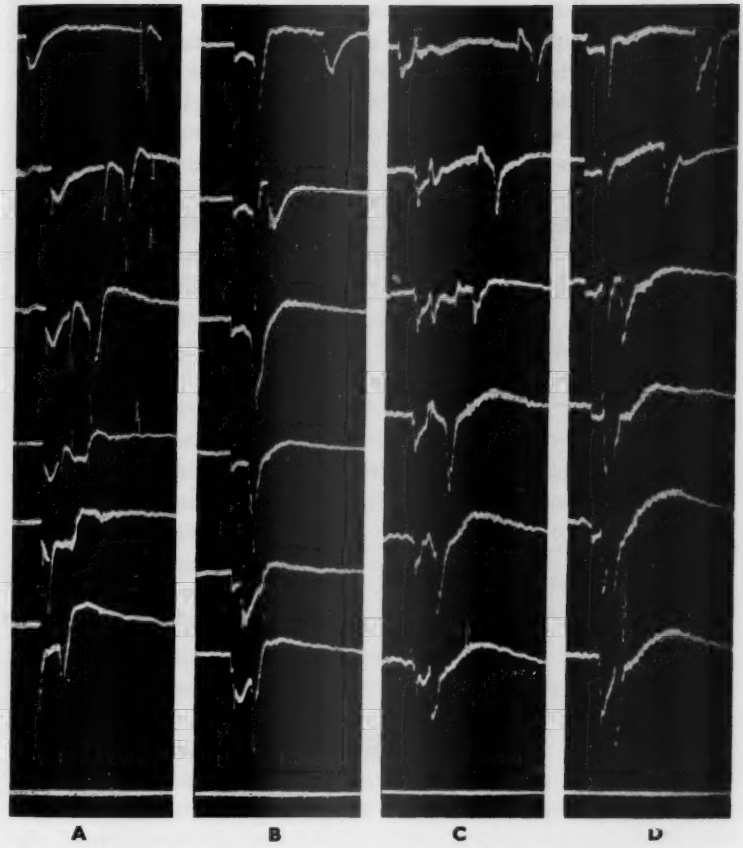


Fig. 30. Interaction between pontine and cortical impulses to contralateral paramedian lobule. Interval between conditioning and test stimuli in msec. below each record. The test response in the top records of all columns was equal to the unconditioned response. — (A) Conditioning response, simple positive wave evoked from pons. Test response, long-latency potential from posterior sigmoid gyrus. — (B) Same as (A) in reversed sequence. — (C) Conditioning response, combined short- and long-latency potential evoked by pontine stimulation. Test response, long-latency potential from anterior sigmoid gyrus. — (D) Same as (C) in reversed order.

sigmoid gyrus. The test response was not influenced until the interval between the stimuli was less than 30 msec. At stimulus intervals of 20 and 10 msec. the test response was greatly depressed, but at the short intervals, less than 5 msec., the test response reappeared, and in the last record (interval 0) it regained its original size.

In column B the same potentials are shown as in A, but in this experiment the ponto-cerebellar potential is the test response. This was apparently little influenced by the conditioning response except when the conditioning and test responses appeared simultaneously (stimulus intervals 25 and 20 msec.). In these records the size of the test response is difficult to evaluate as the two potentials are superposed on each other. At a 20 msec. interval, however, there seems to be a definite decrease in both amplitude and duration of the test response. At a 10 msec. interval the long-latency conditioning response was greatly depressed by the pontine test response. In the last record the conditioning response reappeared as in column A.

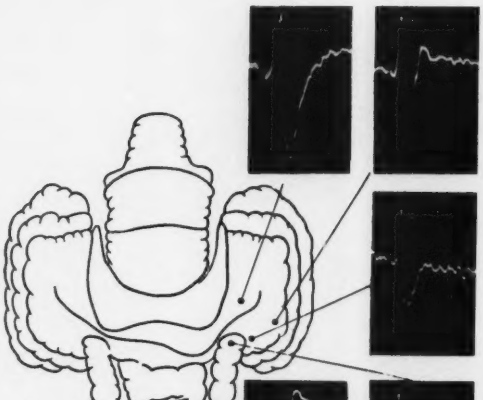


Fig. 31. Responses in contralateral cerebellar hemisphere to stimulation of inferior olivary nucleus.

In column C the conditioning response was evoked by stimulation of the pontine nuclei and consisted of both short- and long-latency components. The test response was a long-latency potential elicited from the anterior sigmoid gyrus. The test response was considerably depressed already at a 50 msec. stimulus interval. The depression was more pronounced in the following record (35 msec.), but at 15 and 8 msec. stimulus intervals there was some increase in the size of the test response.

Column D shows that the long-latency deflection of the same ponto-cerebellar response was greatly depressed by the conditioning long-latency response elicited from the anterior sigmoid gyrus. The depressing effect was evident already at a stimulus interval of 65

msec. As in column B, the short-latency component of the test response was little influenced except perhaps at the short intervals (10,8 msec.).

(2) Inferior olive

The cerebellar responses evoked by stimulation of the inferior olivary complex differed conspicuously from those elicited from the pontine nuclei. As seen in fig. 31 the olivo-cerebellar responses were characterized by quite sharp, prominent deflections with latencies of 3–5 msec. As a rule the potentials were biphasic (negative-positive) or triphasic (negative-positive-negative) when recorded from the cerebellar surface. The initial negative deflection proved to have a lower threshold than the succeeding positive one (fig. 33A). Especially in the posterior two thirds of the paramedian lobule a biphasic (positive-negative) potential was encountered which was found only rarerly in the other lobules of the cerebellar hemisphere. In full harmony with current anatomical knowledge (Brodal 1940) olivo-cerebellar potentials were found in all parts of the hemispheres examined in the present study (paramedian lobule, crus I and II, and posterior part of dorsal paraflocculus) as well as in the vermis of the posterior lobe. The high-amplitude responses were found in the contralateral hemisphere, but smaller ipsilateral responses were also present. No attempt was made to demonstrate the relation between the different subdivisions of the olivary complex and the various parts of the cerebellum.

In order to compare the characteristics of the olivo-cerebellar responses with those elicited from the cerebral cortex and the pontine nuclei, asphyxiation of the animal, local application of strychnine and novocaine, double shock stimulation and interaction experiments between cortical and olivary impulses were carried out.

The effect of *asphyxiation* upon an olivo-cerebellar potential is illustrated in fig. 32. The control response (top record) was a typical triphasic potential. At first a small increase occurred in the positive component (cf. fig. 8). After 2 minutes of asphyxiation a progressive decrease of the positive deflection was observed and after 4 minutes it was completely blocked. The initial negative deflection was still present after 5 minutes, but disappeared after 6 minutes of asphyxiation.

Local *strychninization* had a surprisingly small effect upon the olivo-cerebellar potentials. Sometimes a small decrease in the amp-

litude of the response was observed. Strychnine never significantly enhanced the olivo-cerebellar responses. Following local *novocaine* application, however, the cerebellar responses to olivary stimulation were definitely reduced. The positive deflection was first depressed, whereas the initial negative component was more resistant to the action of this drug.

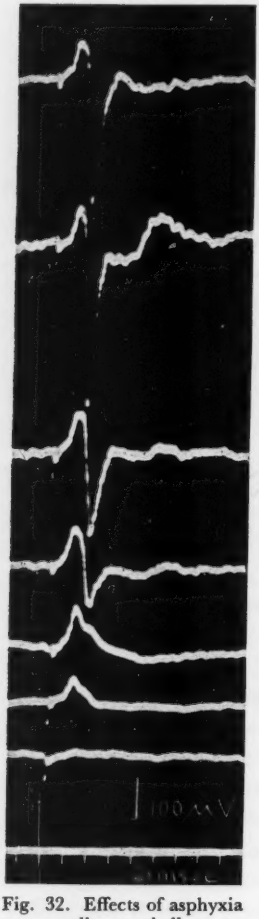


Fig. 32. Effects of asphyxia upon olivo-cerebellar response. Top record, control. Duration of asphyxia indicated in minutes below following records.

Further differences between the negative and positive deflections of the olivo-cerebellar responses were demonstrated by the effect of *double shock stimulation* with varying intervals. The positive deflection of the ordinary negative-positive olivo-cerebellar response was definitely depressed at a 65 msec. shock-interval (fig. 33B). The negative component, on the other hand, had a much shorter unresponsive time and was not significantly depressed at 20 msec. interval. The effect of increasing the stimulus strength of the conditioning shock is illustrated in column C of the same figure. Apparently the positive component of the conditioning response was responsible for the depression of the positive deflection of the test response.

Olivo-cerebellar responses displaying only a slight depression following a conditioning shock were also occasionally encountered (fig. 33D). The second response was a little depressed at a 140 msec. interval, but as the interval between the stimuli was reduced no further depression was observed. Dow (1939) also called attention to the fact that some olivo-cerebellar responses are less readily blocked by previous stimulation than others.

Interesting observations were made in experiments dealing with the *interaction of cortical and olivary impulses* to the cerebellar hemisphere (fig. 34). A long-latency cortical test response was comparatively little

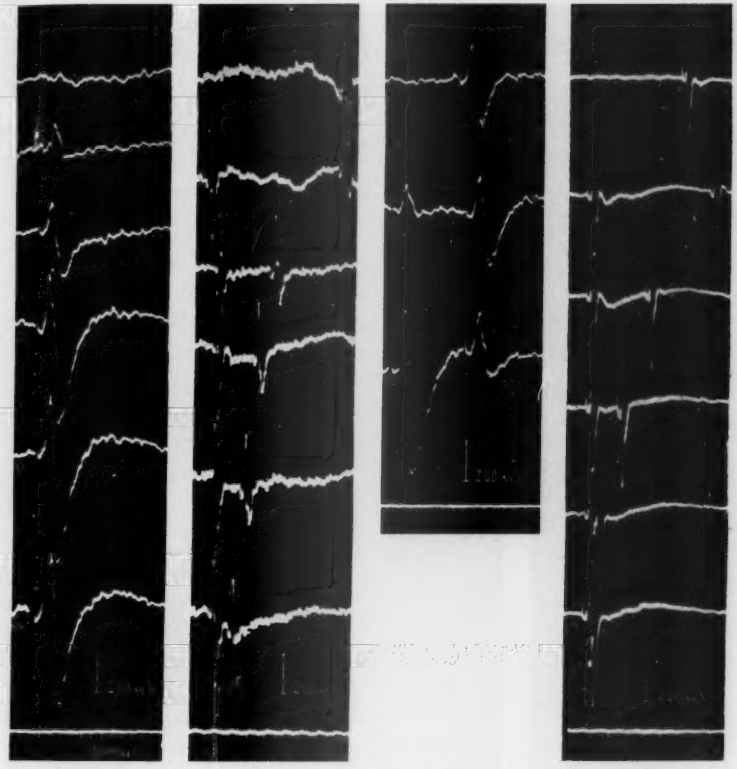


Fig. 33. Cerebellar responses to double shock olivary stimulation. — (A) Effects of increasing stimulus strength. Responses in crus I to stimulation of contralateral olive. Stimulus strength in arbitrary units below each record. — (B) Responses in contralateral crus II to double shock stimulation of olive. Top record, unconditioned response. Interval between shocks in msec. below each record. — (C) Same response as A. Effects of increasing conditioning stimulus strength. Top record, unconditionep response. Conditioning stimulus strength in arbitrary units below 2nd and 3rd record. — (D) Responses in contralateral paramedian lobule. Top record, unconditioned response. Stimulus intervals in msec. below each record.

depressed by a conditioning olivary shock (fig. 34A). No definite depression was observed at 140 and 120 msec. intervals. At a 45 msec. interval the amplitude of the test response was reduced to about one half of the unconditioned response. At shorter intervals (18 and 8 msec.) there was a small increase in the test response.

An olivary test response, on the other hand, displayed an obvious depression following a cortical conditioning shock (fig. 34B). A

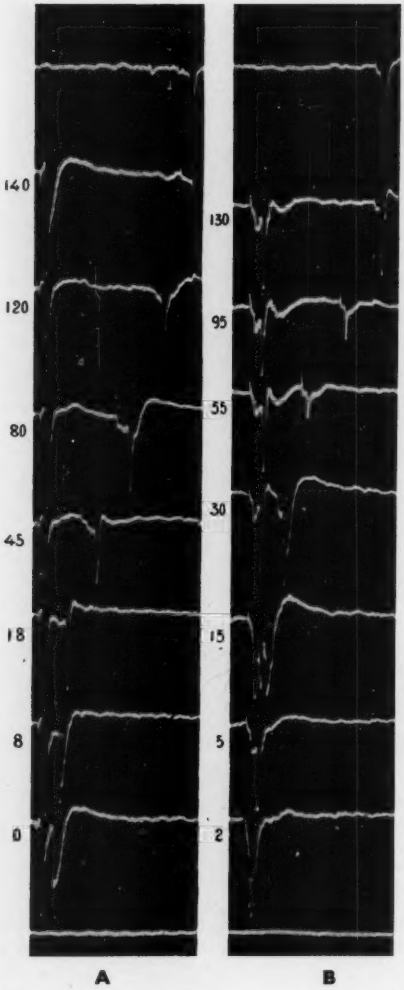


Fig. 34. Interaction between olivary and cortical impulses to contralateral paramedian lobule. — (A) Conditioning response evoked from olive. Test response, long-latency potential from anterior sigmoid gyrus. — (B) Same as (A) in reversed sequence. Top records, unconditioned responses. Shock intervals in msec. below each record.

definite depression was observed already at a 130 msec. interval. At 95 and 55 msec. intervals the test response was almost completely blocked, but at still shorter intervals (30 and 15 msec.) an increase occurred in the amplitude of the test response. At a 5 msec. interval the two responses appeared simultaneously, and it is seen that the test response was occluded, suggesting a convergence of the impulses upon common final elements.

(3) PERIAQUAEDUCTAL GRAY SUBSTANCE

In order to compare the cerebellar impulses relayed through the inferior olive with the cortico-cerebellar impulses already described (chapter III), certain brain stem nuclei were stimulated. Walberg's investigation (1956) of the descending paths to the inferior olive, mentioned in some detail in chapter I, served as a guide in selecting the nuclei for stimulation. Stimulation of these brain stem nuclei were considered desirable also as control of the findings of Walberg by a different method, viz. the technique of evoked potentials.

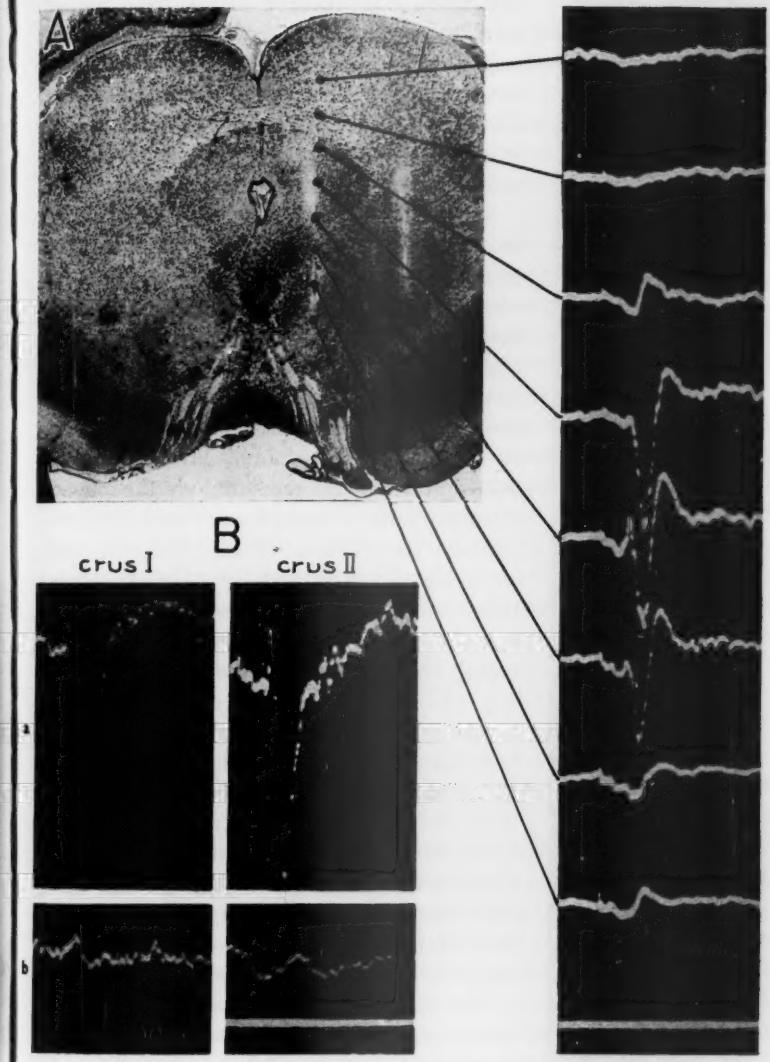
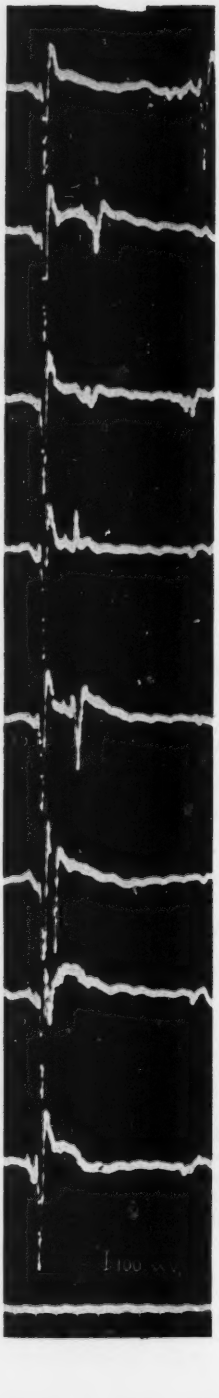


Fig. 35. Cerebellar responses to stimulation of mesencephalon. — (A) stimulated points (1 mm apart) and corresponding responses obtained in the contralateral crus I. From electrode track, barely visible laterally in the section, no response were obtained in the cerebellum. — (B) Contralateral (a) and ipsilateral (b) responses in crus I and crus II to stimulation of point 4 from above in section in (A).



Following stimulation of the head of the caudate nucleus and the nucleus ruber, no responses were obtained in the contralateral cerebellar hemisphere, particularly not in the crus I, although good responses were obtained in the cerebellum following excitation of the cerebral cortex in the same preparations.

Stimulation of the mesencephalon in the region of the periaquaeductal gray substance elicited conspicuous responses in the contralateral cerebellar hemisphere (fig. 35). All these cerebellar responses were abolished after a complete midsagittal section of the medulla between the two olives, although the animal remained in fairly good condition. It appears highly probable, therefore, that these impulses were mediated via the inferior olivary nucleus. In agreement with the conclusions of Walberg (1956), the responses were found contralaterally in all the cerebellar lobules examined (paramedian, crus I and II of the ansiform and the dorsal paraflocculus). No ipsilateral responses were observed (fig. 35). The ventral parts of the periaquaeductal gray proved to be the most efficient activating zone in complete accordance with the findings of Walberg. Similar responses were also occasionally elicited more caudally in the mesencephalon by stimulation of points in the reticular formation ventral to the periaquaeductal gray. This may possibly be due to stimulation of the fibres which pass from the periaquaeductal gray to the inferior olive.

The cerebellar responses elicited by stimulation of the periaquaeductal gray were remarkably similar to those evoked from the

Fig. 36. Effects of double shock stimulation of periaquaeductal gray substance. Records from crus I. Second response in top record equal to unconditioned response. Shock intervals in msec. below each record.

olive. The latencies, however, of the former were from 7–12 msec. to the major deflection, whereas the latter had latencies from 3–5 msec. The potential as a rule consisted of a quite sharp negative deflection succeeded by a positive component and occasionally by a late surface-negative wave, but pure positive or negative potentials were also encountered. As was the case following olivary stimulation the pure positive potentials were most frequently found in the posterior part of the paramedian lobule.

Double shock stimulation of the periaquaeductal gray showed that these impulses always were extremely sensitive to conditioning by previous activity (fig. 36). The second response was often completely blocked up to 70 msec. after the conditioning shock. The reappearance of the test response at shorter intervals was also a constant phenomenon in these experiments. In the experiment shown in fig. 36 the second response was greatly reduced at a 50 msec. interval and almost completely blocked at 45 msec. At 35 msec. there was a partial block of the second response. At still shorter intervals (15 msec.) there appeared a certain increase in the amplitude of the test response. At a 10 msec. interval it was again greatly reduced. It is of interest that the recovery cycle of these responses elicited from the periaquaeductal gray are quite similar to those of the long-latency cortico-cerebellar responses mediated via the pontine nuclei.

(4) Discussion

Pons. — On stimulating deep cerebral structures by means of penetrating electrodes it is difficult to know exactly which elements are excited. As regards the pontine stimulations carried out in this investigation it is believed that the impulses originated in the pontine nuclei. The points which gave rise to the typical short-latency response were always found to be located within the pons (fig. 26). The threshold of the pontine response corresponded quite closely to the threshold of the responses from the cerebral cortex and from the periaquaeductal gray and the inferior olive. The extremely short latency of the responses elicited from the pons suggests that the impulses are mediated to the cerebellum via direct fibres. A lesion of the restiform body did not influence the response elicited

from the pons. Following lesions of the pontine brachium, however, it was immediately abolished (figs. 27, 28). The short latency and the effect of these brain stem lesions eliminate the possibility that the cerebellar responses to pontine stimulation are due to activation of, for instance, fibres passing to the olive.

As regards the form and distribution of the cerebellar potentials evoked by pontine stimulation the results of the present study are to a great extent in agreement with those of Dow (1939). The responses are found in all parts of the cerebellar hemisphere studied. It proved impossible to detect variations in the distribution of the potentials following stimulation of different points in the pons. As also maintained by Dow the responses generally consist of an initial sharp spike of very short latency followed by a broad wave. Dow did not, however, describe the long-latency component observed in the present study.

Based on the experiments described above and the interpretation of the cortico-cerebellar evoked potentials, one may venture the following suggestions as to the origin of the different components of the ponto-cerebellar evoked potentials. The initial spike-like component is presumably due to activity in the ponto-cerebellar fibres. In favour of this interpretation are (i) the very short latency of the response (1–2 msec.), (ii) the short duration of the spike-component (1–3 msec.) and (iii) its resistance to local application of strychnine and novocaine (fig. 27). The experiments with asphyxiation were equivocal. If the above conclusion is correct, the pontine neurons and the cerebellar elements giving origin to the broad wave must be approximately equally sensitive to asphyxia (fig. 28).

The short-latency broad wave of the ponto-cerebellar evoked potentials appears to correspond to the short-latency component of the cortico-cerebellar potentials which has been attributed to activity in the granule cells (chapter III). The following observations favour this interpretation: (i) the shape and time relations of the two potentials are remarkably similar; (ii) both display a short unresponsive time on double shock stimulation (fig. 29); (iii) in interaction experiments, furthermore, both have a relatively long-lasting depressing effect on the long-latency deflection of the cortico-cerebellar potentials; finally, (iv) both are little influenced by a conditioning cortico-cerebellar long-latency potential (figs. 10 and 30). (v) In the asphyxiation experiments both the pontine and cortical short-latency potentials displayed a greater resistance to

asphyxia than the corresponding long-latency components (figs. 8 and 28). Following strychninization, however, the changes taking place in the ponto-cerebellar and cortico-cerebellar short-latency potentials were not quite similar. At first there was a depression of both potentials (figs. 6 and 27), but the increase observed in the ponto-cerebellar potentials after prolonged strychninization (fig. 27) was not observed in the cortico-cerebellar short-latency potentials. The reason for this apparent discrepancy may perhaps be that the granule cells are activated in a different way when the pontine nuclei are stimulated directly.

The sharp long-latency deflection of the cerebellar evoked potentials is not constantly seen following pontine stimulation. This deflection has a higher threshold than the short-latency wave, and it was not described by Dow (1939). At present no explanation can be offered as to why the long-latency deflection is so inconstant in the ponto-cerebellar potentials. The shape and time relations of this component suggest that it corresponds to the long-latency cortico-cerebellar potentials. The low resistance to asphyxia displayed by this deflection lends support to this assumption (fig. 28B). The interaction experiments, furthermore, demonstrated that it is depressed for a considerable time following a conditioning long-latency cortico-cerebellar potential (fig. 30D) as one would expect if the interpretation suggested above is correct.

The conclusion is ventured, therefore, that the long-latency deflection of the ponto-cerebellar evoked potentials probably represents activity in the Purkinje cells.

On comparing the interaction experiments in fig. 30A and C it is evident that the test response is depressed for a longer period of time in the latter case. This indicates that the long-latency deflection present in the conditioning ponto-cerebellar response of C is responsible for the depression appearing at long intervals (50, 35 msec.) as well as for the small increase in the amplitude of the test response at shorter intervals (15, 8 msec.). The depressing effect of the pure short-latency potential, on the other hand, lasted less than 30 msec. (column A).

The finding of ipsilateral ponto-cerebellar responses does not necessarily signify the existence of ipsilateral ponto-cerebellar fibres, although such connections have been shown to exist (Brodal and Jansen 1946), but may be due to stimulation of axons originating in the other half of the pontine nuclei.

Inferior olive. — The olive was stimulated by means of bipolar (1 mm) electrodes applied to the ventral medullary surface overlying the olive. Care was taken to locate low-threshold points. It is difficult, however, to rule out the possibility that neighbouring structures (eg. the lateral reticular nucleus) were activated simultaneously. But as the cerebellar projection of the lateral reticular nucleus is ipsilateral (Brodal 1943), it is considered likely that the contralateral responses studied in the present investigation were elicited from the inferior olivary nucleus. The ipsilateral cerebellar responses to stimulation in the region of the olive were probably due to either stimulation of axons from the opposite olive or spread of stimulating current to the lateral reticular nucleus.

The form as well as the distribution of the olivo-cerebellar responses observed in the present study conform quite well to the description of Dow (1939). Responses with latencies of 20 msec. found by Combs (1956) in the anterior lobe have not been observed in the cerebellar hemisphere.

The present material does not permit an analysis of the origin of the different components of the olivo-cerebellar responses. However, the total occlusion observed between a long-latency cortical and a surface-positive olivo-cerebellar response (fig. 34B) suggests that they originate in the same elements viz. the Purkinje cells (cf. chapter III A). The similarity in form between the two responses strengthens this suggestion.

Following stimulation in the olivary region with double shocks Dow (1939) as a rule found quite long absolute unresponsive periods (70 msec.). In Dow's experiments the olivary system apparently was stimulated by means of electrodes penetrating from the dorsal surface of the medulla. He suggests that presumably the presynaptic fibres running to the olive were stimulated. On stimulating the olive from the ventral surface of the medulla these long absolute unresponsive periods were rarely observed, possibly because the olivo-cerebellar fibres or their cells of origin were stimulated directly (Dow 1939).

The investigation of the interaction between cortical and olivary impulses to the cerebellum revealed that an olivary test response was depressed to a much greater extent by a cortical conditioning response than vise versa. This suggests that part of the interaction took place in the olive, the excitability of which was depressed for at least 100 msec. following a cortical stimulus. The effect may be

mediated via the cortico-olivary fibres. These observations confirm Dow's (1939) demonstration that the olive was exceedingly sensitive to conditioning by previous activity.

Caudate nucleus and nucleus ruber. — In agreement with the findings of Mettler, Grundfest and Hovde (1952) no responses were obtained in the cerebellar hemispheres following stimulation of the caudate nucleus. Johnson and Snider (1953), on the other hand, observed potentials in the crus II after caudate stimulation in curarized cats. Stimulation of the nucleus ruber also left the cerebellar hemisphere unresponsive in the present study. Based on his silver degeneration studies, Walberg (1956) concludes that the caudate as well as the nucleus ruber project to the crus I via the inferior olive. It goes without saying that the failure to obtain responses in the crus I following stimulation of these two nuclei does not exclude the existence of fibres from the caudate and ruber to the olive.

Periaquaeductal gray substance. — The results of stimulation of the periaquaeductal gray confirmed Walberg's (1956) conclusion that this area projects to the entire contralateral posterior lobe via the inferior olive. Especially the ventral parts of the central gray seems to give origin to the fibres passing to the olive.

Double shock stimulation of the periaquaeductal gray demonstrated that these responses, mediated via the inferior olive, have recovery cycles very similar to the long-latency cortico-ponto-cerebellar responses. The possibility that the long unresponsive period is due to the properties of the cerebellar cortex, therefore, appears likely.

Chapter V

General considerations

In order not to exceed the scope of this article the following considerations are confined to a few major questions on which the afore described observations may shed some light.

Mode of activation of the cerebellar cortex. — The demonstration of different types of responses in the cerebellar hemisphere following stimulation of the cerebral cortex raises the question of the mode of activation of the cerebellar cortex. Considering the cytoarchitecture of this cortex with the characteristic relationship of granular layer and mossy fibres, Purkinje cells and climbing fibres, the following suggestions seem justifiable. To deal first with the short-latency cortico-cerebellar potentials one is led to presume that these potentials represent activity set up in the granule cells by afferent impulses through the mossy fibre system as further elaborated in chapter III A to which the reader is referred. We may then turn to the long-latency potentials, which have been attributed to activity in the Purkinje cells (chapter III A). Two explanations may deserve closer attention in this connection. As demonstrated in chapter III these potentials are generally set up by stimulation of particular areas of the cerebral cortex. They are most readily elicited from the anterior and posterior sigmoid gyri. It is conceivable that stimulation of this pericruciate region may primarily activate granule cells through the mossy fibres in some buried part of the cerebellar cortex which is inaccessible to an exploring surface electrode. If so, the long-latency potential might be the result of an intracortical spread of the activity from the granule cells to the Purkinje cells.

A second possibility is that the pure long-latency potentials represent a primary activation of the Purkinje cells via the climbing fibre system. This would imply that stimulation of different areas of the cerebral cortex may activate different types of cells in the pontine nuclei, viz. (i) cells whose axons terminate as climbing fibres on the Purkinje cells and (ii) cells whose axons form mossy fibres and mediate short-latency potentials. The localized termination and the fine caliber of the climbing fibres may perhaps partly account for the sharp localization and long-latency of the impulses mediated via these fibres as compared to the short-latency potentials mediated via the thicker and more diffusely distributed mossy fibres.

The most recent concept of the origin of the climbing fibres in the cerebellar nuclei (Carrea, Reissig and Mettler 1947) is not easily reconcilable with the suggestion that the pure long-latency cortico-cerebellar potentials are mediated via the climbing fibre system. It is possible, however, that the impulses are relayed from the pontine nuclei via the deep cerebellar nuclei to the cerebellar cortex although such a pathway has not so far been demonstrated (Brodal and Jansen 1946). On the other hand, the question of the origin of the climbing fibres cannot be considered as definitely settled.* As pointed out in chapter I, some early investigators have suggested that all precerebellar nuclei contribute both climbing and mossy fibres to the cerebellar cortex (Jakob 1928, Strong 1929).

The hypothesis of long-latency cortico-cerebellar potentials mediated via the climbing fibres is thus hardly compatible with current anatomical viewpoints, nor is the first explanation, that the long-latency potentials represent relayed granule cell activity, entirely satisfactory. It would imply that the pericruciate cortex (somatic I) activates some granule cells deeply buried in the cerebellar folia whereas for instance the anterior ectosylvian gyrus (somatic II) activates granule cells close to the cerebellar surface. This supposition seems rather far-fetched and it does not harmonize with the observation that the long-latency potentials display a sharper localization than do the short-latency ones. The climbing fibres, on the other hand, appear to be better suited for the transmission of localized responses.

* The existence of climbing fibres in the pontine brachium has also been suggested by Granit and Phillips (1956) in a publication which appeared while the present paper was in press.

To sum up, the present investigation does not permit a definite answer to the question whether the pure long-latency potentials represent a primary activation of Purkinje cells or relayed granule cell activity. Recording of the antidromic activity set up in the pontine nuclei following stimulation of the cerebellar cortex might perhaps yield critical information on this point.

The present study also demonstrates certain differences between sensory somatic areas I and II of the cerebral cortex. As yet little insight has been gained concerning the functional rôle played by the respective areas. As mentioned above, stimulation of somatic area I as a rule evokes well-localized long-latency responses in the paramedian lobule, whereas more diffuse short-latency responses are elicited from the somatic area II. This is consistent with the demonstrations of a more detailed localization within the somatic area I than within the somatic area II of the cerebral cortex (Woolsey and Fairman 1946). In the somatic area II there is a bilateral sensory representation of the body surface whereas only contralateral responses are obtained in the sensory somatic area I on peripheral stimulation. In the present study, however, bilateral paramedian responses were obtained as readily from the somatic area I as from somatic area II.

Functional localization in the cerebellar hemisphere. — It was shown in chapter III B that the different lobules of the cerebellar hemisphere to a certain extent are related to different parts of the cerebral cortex. This relationship presumably signifies a certain degree of functional localization in the hemispheres of the cerebellum.

To a great extent inspired by the comparative anatomical work of Bolk (1906) numerous investigators have endeavoured to demonstrate a definite somato-topical localization within the cerebellar hemisphere by means of ablation and stimulation experiments. In more recent years, however, the elaborate functional subdivision of the cerebellum described by, for instance, van Rijnberk (1926) and Mussen (1927) has been extensively critizised (see reviews by Fulton and Dow 1937 and Carrea and Mettler 1947). Fulton and Dow as well as Carrea and Mettler concluded that no functional differences can be demonstrated between the lobules of the cerebellar hemisphere.

The most recent contribution to the study of localization within

the cerebellar hemisphere appears to be the extensive investigations of Chambers and Sprague (1955a, b). Substantiating the anatomical observations of Jansen and Brodal (1940, 1942) these authors subdivide the entire cerebellum into three longitudinal zones related to the fastigial, interposed and dentate nuclei respectively. On the basis of stimulation and ablation experiments they assign different functional properties to the three longitudinal zones. Dealing with the cerebellar hemisphere, it is of particular interest that Chambers and Sprague consider the paramedian lobule as a part of the intermediate zone whereas the rest of the hemisphere viz. crus I and II of the ansiform lobule and the paraflocculus belong to the lateral zone. In the intermediate zone there appears to be a definite somato-topic localization. Within the lateral zone, however, Chambers and Sprague were unable to demonstrate any such localization.

In the present study responses were obtained in the dorsal *paraflocculus* following stimulation of certain well circumscribed cortical zones only (figs. 13, 14). These cortical areas coincided quite closely with cortical zones yielding autonomic effects on stimulation (cf. chapter III B). Recently Walberg (1956) suggested that the paraflocculus may somehow be associated with regulation of autonomic activities on account of the massive projection of the periaquaeductal gray via the inferior olive onto the paraflocculus. The close relationship between the periaquaeductal gray and the paraflocculus was demonstrated in the present study as well (chapter IV, part 3). However, the periaquaeductal gray was likewise found to project onto the rest of the cerebellar hemisphere. Hence possible autonomic impulses from this source would be distributed to the entire hemispheral part of the posterior lobe. Stimulation of the paraflocculus has as yet yielded little to unveil the functional significance of this lobule. Based on ablation experiments Ten Cate (1926) and Scholten (1946) conclude that the paraflocculus contributes to the maintenance of tone in the ipsilateral extremities. The extraordinary development of the paraflocculus in whales (Jansen 1950) is hardly compatible with the latter conclusion, nor do the experiments of Chambers and Sprague (1955b) lend support to this conception.

In the present investigation the anterior and posterior parts of the dorsal and the ventral paraflocculus were activated from different areas of the cerebral cortex, a fact that presumably indicates a certain functional differentiation within this lobule (figs. 13, 14 and 16). The close correspondance between the cortical zones yiel-

ding parafloccular responses and those from which recruiting responses have been obtained on thalamic stimulation by Starzl and Magoun (1951) makes one speculate whether the paraflocculus is somehow related to the "associational" cortex. Such a relationship might correspond to that between the ansiform lobule and the motor cortex demonstrated by Rossi (1912) and Walker (1938). This would explain the minimal effect of parafloccular lesions (Keller, Roy and Chase 1937; Carrea and Mettler 1947; Chambers and Sprague 1955b) and the doubtful effects obtained on stimulation of this part of the cerebellum (Dow 1935). The possible existence of a relationship between the paraflocculus and the "associational" cortex should lend itself to experimental testing.

Turning to the *ansiform lobule* there exists at present no definite information as regards the functional significance of this lobule. Bolk (1906) advanced the hypothesis that the ansiform lobule acted as a coordination center for the ipsilateral extremities. This view was supported by van Rijnberk (1926) and Scholten (1946). These authors suggested from ablation experiments that the crus I controlled forelimb and the crus II hindlimb activities. Larsell and von Berthelsdorf (1941) brought forward comparative anatomical data in support of this hypothesis. However, recent investigators have not been able to demonstrate such a relationship (Keller, Roy and Chase 1937; Botterell and Fulton 1938; Carrea and Mettler 1947; Chambers and Sprague 1955b). Walberg (1956) has pointed out that the two crura of the ansiform lobule differ with regard to afferent connections. Whereas the crus II may be influenced from the cortex cerebri via the inferior olive, the crus I seems to receive subcortical impulses only, through the olive. The more intimate association of the crus II with the cerebral cortex is also emphasized by the present investigation. Following cortical stimulation, responses were more readily obtained in the crus II than in crus I. Furthermore, the extent of cortical surface yielding responses in crus II exceeded by far that activating the crus I. It has been suggested that the ansiform lobule subserves "head functions" (Hampson 1949; Hampson, Harrison and Woolsey 1950; Woolsey 1950). The present study demonstrates, however, that fore- and hindleg subdivisions of the motor cortex and the somatic area II as well as the head-face subdivisions of the same areas may activate crus II. The possibility of spinal impulses reaching the ansiform lobule via the pontine nuclei (Walberg and Brodal 1953) also

deserves to be mentioned in this connection. The responses from the medial part of the motor cortex (hindleg subdivision) and the posterior part of the somatic area II (hindleg subdivision) were especially found in the lateral part of crus II whereas the medial part was more readily activated from face subdivisions. This suggests a certain degree of localization within the crus II (figs. 17 and 18). Chambers and Sprague (1955b) have emphasized the necessity of distinguishing between the ansiform and paramedian lobules on account of their efferent projections. In the present study of the cortical afferent connections to the respective lobules, the striking difference between them is the lack of ansiform responses to stimulation of the posterior sigmoid gyrus (sensory somatic area I). Thus the ansiform lobule seems to be particularly related to the motor areas of the cerebral cortex, as demonstrated by Rossi (1912) and Walker (1938).

In the *paramedian lobule* a definite somatotopic localization appears to exist as described in more detail in chapters I and III B. Stimulation (Hampson, Harrison and Woolsey 1950), and ablation experiments (Chambers and Sprague 1955b) as well as mapping of peripheral afferent impulses (Snider and Stowell 1944) have established a face-foreleg area in the anterior folia and a hindleg area in the posterior folia of this lobule. The same distribution of impulses was demonstrated in the present study following stimulation of the different subdivisions of the motor area as well as the sensory somatic areas I and II (pp. 55-60). Chambers and Sprague (1955b) state that the intermediate zone of the cerebellum, including the paramedian lobule, controls the postural placing and hopping reflexes, tone and individual movements of ipsilateral limbs. Much work remains in order to clarify in what manner the paramedian lobule exerts its influence upon the different limbs, and through which pathways these effects are mediated.

As is evident from these considerations, our knowledge of the functional significance of the various lobules of the cerebellar hemisphere is still very vague. Localized stimulation experiments, preferably in unanaesthetized animals, with a careful study of the effects upon the activity in the cerebral cortex, in the reticular formation and in the spinal cord appear to be the most promising approach in the future to shed light on this particular problem.

Summary

1. The present investigation is concerned with the afferent impulses to the cerebellar hemisphere in cat from the cerebral cortex, the pontine nuclei, the inferior olive and the periaquaeductal gray.

2. Three types of cortico-cerebellar potentials are described viz. short-latency, long-latency and combined short- and long-latency potentials (chapter III A).

3. The cortico-cerebellar responses seem to be mediated via the pontine nuclei under the prevailing experimental conditions (chapter III C).

4. Certain characteristics of the different types of responses have been revealed by means of records from the different layers of the cerebellar cortex, local application of strychnine and novocaine, asphyxiation, double shock stimulation with varying shock intervals and interaction between different impulses to the same cerebellar point (chapter III A).

5. The possible origin of the various types of responses in different elements of the cerebellar cortex has been discussed. It is suggested that (i) the short-latency potential represents activity in the granular layer, (ii) the long-latency potential originates in the Purkinje cells and, (iii) the late surface-negative wave is due to activity in the Purkinje cell dendrites (chapter III A).

6. The distribution and extent of the cortical areas yielding responses in the different cerebellar lobules (dorsal and ventral paraflocculus, crus I and II of the ansiform lobule and the paramedian lobule) have been mapped.

Under the prevailing experimental conditions the various cerebellar lobules, or even parts of them, appeared to be activated to

a certain extent from different parts of the cerebral cortex (chapter III B).

7. Stimulation of the pontine nuclei yielded responses in all parts of the cerebellar hemisphere examined (paramedian and ansiform lobules and dorsal paraflocculus).

These responses consisted of a short-latency initial spike followed by a slow wave and sometimes a long-latency sharp deflection (chapter IV).

8. It is suggested that the initial spike represents activity in the ponto-cerebellar fibres, the slow wave is assigned to activity in the granular layer and the long-latency deflection represents Purkinje cell activity (chapter IV).

9. Stimulation of the inferior olive evoked potentials in all explored cerebellar lobules (paramedian and ansiform lobules and dorsal paraflocculus).

These responses differed conspicuously from the ponto-cerebellar ones. However, the data obtained in the present investigation do not permit an analysis of these responses with regard to the origin of the different components (chapter IV).

10. Stimulation of the periaquaeductal gray elicited responses in all examined lobules of the contralateral cerebellar hemisphere. These potentials were mediated via the inferior olive and their form was similar to the olivo-cerebellar responses (chapter IV).

11. The mode of activation of the cerebellar cortex by the afferent impulses and the bearing of the present observations upon the question of cerebellar localization are briefly discussed (chapter V).

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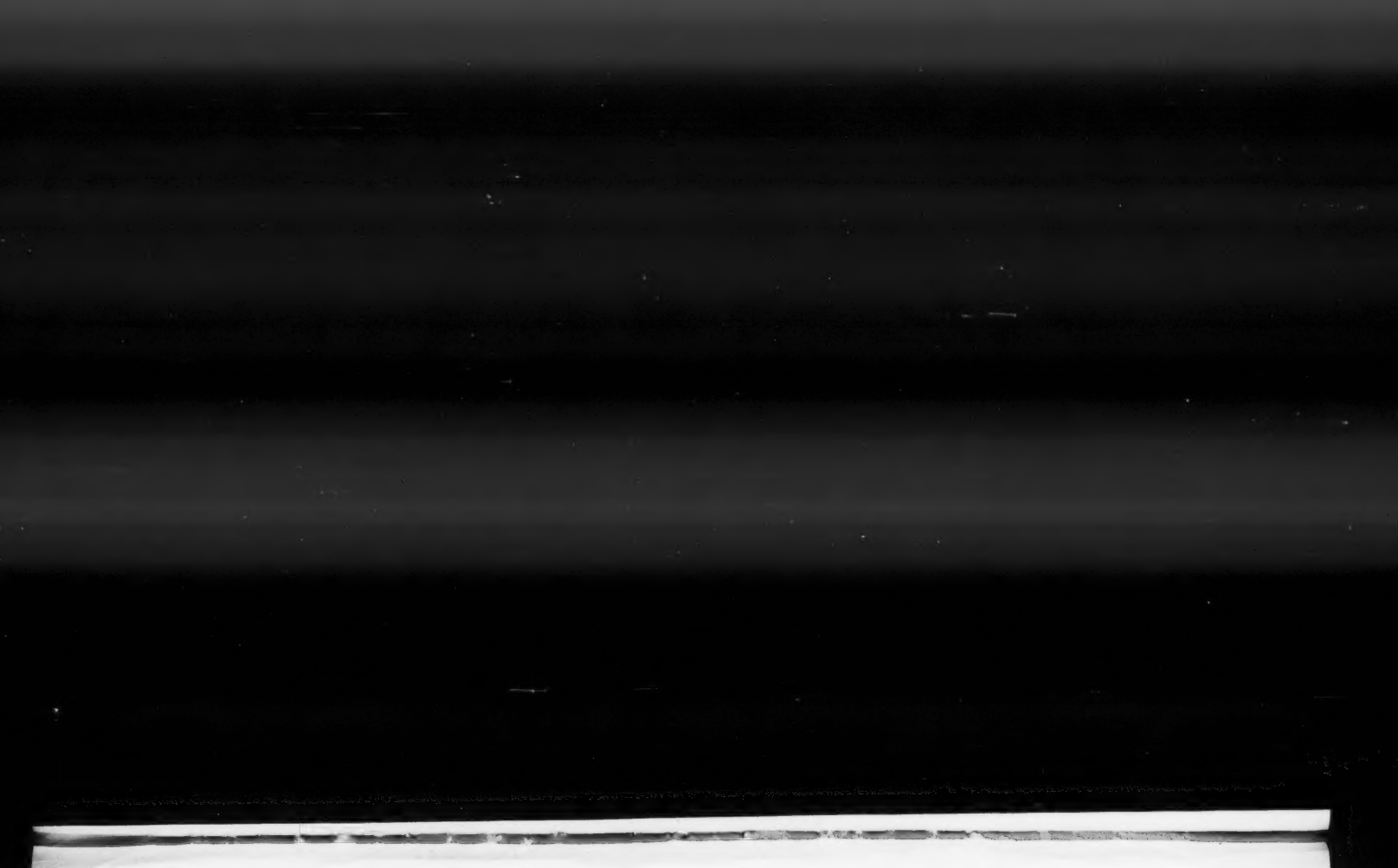
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